#### s263US104.ST25 SEQUENCE LISTING

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DERAND, Renaud
GARCIA, Elisabeth
PROST. Anne-Lise

REVILLOUD, Jean VIVAUDOU, Michel

- <120> ION CHANNEL HYBRID PROTEINS AS ELECTRICAL SENSORS AND USE THEREOF
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- <160> 25
- <170> PatentIn version 3.1
- <210> 1
- <211> 1927 <212> PRT
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Gln Glu His Thr Lys Val Arg Leu Ser Val Tyr Gly Ala Leu Gly 1010 1015

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Gly Gln Arg Phe Val Pro Ile Val Ala Glu Glu Asp Gly Arg Tyr 1850 1860

1630

Page 8

s263uS104.ST25 Ser Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile Lys Val Pro Thr 1865 1870 1875 Pro Leu Cys Thr Ala Arg Gln Leu Asp Glu Asp Arg Ser Leu Leu 1880 1885 1890 Asp Ala Leu Thr Leu Ala Ser Ser Arg Gly Pro Leu Arg Lys Arg Ser Val Ala Val Ala Lys Ala Lys Pro Lys Phe Ser Ile Ser Pro Asp Ser Leu Ser 1925 <210> 2 <211> 1911 <212> PRT <213> Saccharomyces cerevisiae <400> 2 Met Ala Gly Asn Leu Val Ser Trp Ala Cys Lys Leu Cys Arg Ser Pro 1 10 15 Glu Gly Phe Gly Pro Ile Ser Phe Tyr Gly Asp Phe Thr Gln Cys Phe Ile Asp Gly Val Ile Leu Asn Leu Ser Ala Ile Phe Met Ile Thr Phe Gly Ile Arg Asp Leu Val Asn Leu Cys Lys Lys Lys His Ser Gly Ile

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1103 1170

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Met Val Trp Trp Leu Ile Ala Phe Ala His Gly Asp Leu Ala Pro 1610 1620 Page 15

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Leu Cys Thr Ala Arg Gln Leu Asp Glu Asp Arg Ser Leu Leu Asp 1865 1870 1875 Ala Leu Thr Leu Ala Ser Ser Arg Gly Pro Leu Arg Lys Arg Ser 1880 1885 1890 Val Ala Val Ala Lys Ala Lys Pro Lys Phe Ser Ile Ser Pro Asp

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Trp Gly Ser Gln Ser Ser Lys Val Gln Ile His His Asn Thr Trp Leu

His Phe Pro Gly His Asn Leu Arg Trp Ile Leu Thr Phe Ala Leu Leu 65 70 75 80 Phe Val His Val Cys Glu Ile Ala Glu Gly Ile Val Ser Asp Ser Gln

Arg Ala Ser Arg His Leu His Leu Phe Met Pro Ala Val Met Gly Phe  $100 \hspace{1cm} 105 \hspace{1cm} 110$ 

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Arg Leu Arg Pro Ala Glu Thr Glu Asp Val Ala Ile Lys Val Thr Asn  $660 \hspace{0.5cm} 665 \hspace{0.5cm} 665$ Gly Tyr Phe Ser Trp Gly Ser Gly Leu Ala Thr Leu Ser Asn Ile Asp 685 685 ile Arg ile Pro Thr Gly Gln Leu Thr Met ile Val Gly Gln Val Gly 690 695 700 Cys Gly Lys Ser Ser Leu Leu Leu Ala Ile Leu Gly Glu Met Gln Thr 705 710 720 Leu Glu Gly Lys Val Tyr Trp Asn Asn Val Asn Glu Ser Glu Pro Ser 725 730 735 Phe Glu Ala Thr Arg Ser Arg Ser Arg Tyr Ser Val Ala Tyr Ala Ala 740 745 750 Gln Lys Pro Trp Leu Leu Asn Ala Thr Val Glu Glu Asn Ile Thr Phe 755 760 765 Gly Ser Ser Phe Asn Arg Gln Arg Tyr Lys Ala Val Thr Asp Ala Cys 770 780 Ser Leu Gln Pro Asp Ile Asp Leu Leu Pro Phe Gly Asp Gln Thr Glu 785 790 795 Ile Gly Glu Arg Gly Ile Asn Leu Ser Gly Gly Gln Arg Gln Arg Ile 805 810 815 Cys Val Ala Arg Ala Leu Tyr Gln Asn Thr Asn Ile Val Phe Leu Asp 820 825 830 Asp Pro Phe Ser Ala Leu Asp Ile His Leu Ser Asp His Leu Met Gln 835 Glu Gly Ile Leu Lys Phe Leu Gln Asp Asp Lys Arg Thr Val Val Leu 850 860 Val Thr His Lys Leu Gln Tyr Leu Thr His Ala Asp Trp Ile Ile Ala 865 870 875 880 Met Lys Asp Gly Ser Val Leu Arg Glu Gly Thr Leu Lys Asp Ile Gln 885 890 895 Thr Lys Asp Val Glu Leu Tyr Glu His Trp Lys Thr Leu Met Asn Arg 900 905 910 Page 20

Gln Asp Gln Glu Leu Glu Lys Asp Met Glu Ala Asp Gln Thr Thr Leu Glu Arg Lys Thr Leu Arg Arg Ala Met Tyr Ser Arg Glu Ala Lys Ala 930 935 940 Gln Met Glu Asp Glu Asp Glu Glu Glu Glu Glu Glu Asp Glu Asp 945 950 955 960 Asp Asn Met Ser Thr Val Met Arg Leu Arg Thr Lys Met Pro Trp Lys Thr Cys Trp Trp Tyr Leu Thr Ser Gly Gly Phe Phe Leu Leu Phe Leu 980 985 990 Met Ile Phe Ser Lys Leu Leu Lys His Ser Val Ile Val Ala Ile Asp Tyr Trp Leu Ala Thr Trp Thr Ser Glu Tyr Ser Ile Asn Asp Pro Gly Lys Ala Asp Gln Thr Phe Tyr Val Ala Gly Phe Ser Ile Leu Cys Gly Ala Gly Ile Phe Leu Cys Leu Val Thr Ser Leu Thr Val  $1040 \ \ \, 1045$ Glu Trp Met Gly Leu Thr Ala Ala Lys Asn Leu His His Asn Leu 1055 1060 1065 Leu Asn Lys Ile Ile Leu Gly Pro Ile Arg Phe Phe Asp Thr Thr Pro Leu Gly Leu Ile Leu Asn Arg Phe Ser Ala Asp Thr Asn Ile 1085 1090 1095 Ile Asp Gln His Ile Pro Pro Thr Leu Glu Ser Leu Thr Arg Ser Thr Leu Cys Leu Ser Ala Ile Gly Met Ile Ser Tyr Ala Thr 1115 1120 1125 Pro Val Phe Leu Ile Ala Leu Ala Pro Leu Gly Val Ala Phe Tyr 1130 1135 1140 Phe Ile Gln Lys Tyr Phe Arg Val Ala Ser Lys Asp Leu Gln Glu

Leu Asp Asp Ser Thr Gln Leu Pro Leu Leu Cys His Phe Ser Glu Thr Ala Glu Gly Leu Thr Thr Ile Arg Ala Phe Arg His Glu Thr Arg Phe Lys Gln Arg Met Leu Glu Leu Thr Asp Thr Asn Asn Ile Ala Tyr Leu Phe Leu Ser Ala Ala Asn Arg Trp Leu Glu Val Arg Thr Asp Tyr Leu Gly Ala Cys Ile Val Leu Thr Ala Ser Ile Ala Ser Ile Ser Gly Ser Ser Asn Ser Gly Leu Val Gly Leu Gly Leu
1235 1240 1245 Leu Tyr Ala Leu Thr Ile Thr Asn Tyr Leu Asn Trp Val Val Arg 1250 1260Asn Leu Ala Asp Leu Glu Val Gln Met Gly Ala Val Lys Lys Val 1265 1270 1275 Asn Ser Phe Leu Thr Met Glu Ser Glu Asn Tyr Glu Gly Thr Met 1280 1290 Asp Pro Ser Gln Val Pro Glu His Trp Pro Gln Glu Gly Glu Ile 1295 1300 1305 Lys Ile His Asp Leu Cys Val Arg Tyr Glu Asn Asn Leu Lys Pro Val Leu Lys His Val Lys Ala Tyr Ile Lys Pro Gly Gln Lys Val 1325 1330 1335 Gly Ile Cys Gly Arg Thr Gly Ser Gly Lys Ser Ser Leu Ser Leu
1340 1345 Ala Phe Phe Arg Met Val Asp Ile Phe Asp Gly Lys Ile Val Ile Asp Gly Ile Asp Ile Ser Lys Leu Pro Leu His Thr Leu Arg Ser 1370 1380

1150

s263US104.ST25 Arg Leu Ser Ile Ile Leu Gln Asp Pro Ile Leu Phe 1385 1390 1395 Ile Arg Phe Asn Leu Asp Pro Glu Cys Lys Cys Thr Asp Asp Arg 1400 1405 1410Leu Trp Glu Ala Leu Glu Ile Ala Gln Leu Lys Asn Met Val Lys Ser Leu Pro Gly Gly Leu Asp Ala Thr Val Thr Glu Gly Gly Glu 1430 1435 1440 Asn Phe Ser Val Gly Gln Arg Gln Leu Phe Cys Leu Ala Arg Ala 1445 1450 1455 Phe Val Arg Lys Ser Ser Ile Leu Ile Met Asp Glu Ala Thr Ala Ser Ile Asp Met Ala Thr Glu Asn Ile Leu Gln Lys Val Val Met Thr Ala Phe Ala Asp Arg Thr Val Val Thr Ile Ala His Arg Val Ser Ser Ile Met Asp Ala Gly Leu Val Leu Val Phe Ser Glu Gly Ile Leu Val Glu Cys Asp Thr Gly Pro Asn Leu Leu Gln His Lys Asn Gly Leu Phe Ser Thr Leu Val Met Thr Asn Lys Gly Gly Gly Gly Gly Met Leu Ser Arg Lys Gly Ile Ile Pro Glu Glu Tyr 1550 1560 Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr Arg 1565 1570 1575 Thr Arg Glu Arg Arg Ala Arg Phe Val Ser Lys Lys Gly Asn Cys

Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu Gln 1595 1600 1605

Asp Val Phe Thr Thr Leu Val Asp Leu Lys Trp Pro His Thr Leu 1610 1620

Page 23

Leu Ile Phe Thr Met Ser Phe Leu Cys Ser Trp Leu Leu Phe Ala 1625 1630 1635 Met Val Trp Trp Leu Ile Ala Phe Ala His Gly Asp Leu Ala Pro 1640 1650 Gly Glu Gly Thr Asn Val Pro Cys Val Thr Ser Ile His Ser Phe 1665 1660 1665 Ser Ser Ala Phe Leu Phe Ser Ile Glu Val Gln Val Thr Ile Gly 1670 1680 Phe Gly Gly Arg Met Val Thr Glu Glu Cys Pro Leu Ala Ile Leu 1685ile Leu Ile Val Gln Asn Ile Val Gly Leu Met Ile Asn Ala Ile 1700 1710 Met Leu Gly Cys Ile Phe Met Lys Thr Ala Gln Ala His Arg Arg 1715 1720 1725 Ala Glu Thr Leu Ile Phe Ser Lys His Ala Val Ile Thr Leu Arg 1730 1740 His Gly Arg Leu Cys Phe Met Leu Arg Val Gly Asp Leu Arg Lys 1745 1750 1755 Ser Met Ile Ile Ser Ala Thr Ile His Met Gln Val Val Arg Lys 1760 1770 Thr Thr Ser Pro Glu Gly Glu Val Val Pro Leu His Gln Val Asp 1775 1780 1785 Ile Pro Met Glu Asn Gly Val Gly Gly Asn Gly Ile Phe Leu Val 1790 1800 Ala Pro Leu Ile Ile Tyr His Val Ile Asp Ser Asn Ser Pro Leu 1805 1810 1815 Tyr Asp Leu Ala Pro Ser Asp Leu His His His Gln Asp Leu Glu 1820 1825 1830 ıle ile val ile Leu Glu Gly val Val Glu Thr Thr Gly ile Thr 1835 1840 1845 Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp Glu Ile Leu Trp Gly 1850 1860 Page 24

Gln Arg Phe Val Pro Ile Val Ala Glu Glu Asp Gly Arg Tyr Ser

Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile Lys Val Pro Thr Pro 1880 1885 1890

Leu Cys Thr Ala Arg Gln Leu Asp Glu Asp Arg Ser 1895 1900 1905

<210> <211> <212>

PRT Homo sapiens

<400> 4

Met Ala Leu Arg Gly Phe Cys Ser Ala Asp Gly Ser Asp Pro Leu Trp

Asp Trp Asn Val Thr Trp Asn Thr Ser Asn Pro Asp Phe Thr Lys Cys

Phe Gln Asn Thr Val Leu Val Trp Val Pro Cys Phe Tyr Leu Trp Ala

Cys Phe Pro Phe Tyr Phe Leu Tyr Leu Ser Arg His Asp Arg Gly Tyr

Ile Gln Met Thr Pro Leu Asn Lys Thr Lys Thr Ala Leu Gly Phe Leu 65 70 75 80

Leu Trp Ile Val Cys Trp Ala Asp Leu Phe Tyr Ser Phe Trp Glu Arg 85 90 95

Ser Arg Gly Ile Phe Leu Ala Pro Val Phe Leu Val Ser Pro Thr Leu

Leu Gly Ile Thr Thr Leu Leu Ala Thr Phe Leu Ile Gln Leu Glu Arg

Arg Lys Gly Val Gln Ser Ser Gly Ile Met Leu Thr Phe Trp Leu Val

Ala Leu Val Cys Ala Leu Ala Ile Leu Arg Ser Lys Ile Met Thr Ala 145 150 160

Leu Lys Glu Asp Ala Gln Val Asp Leu Phe Arg Asp Ile Thr Phe Tyr  $\begin{array}{c} 175 \\ 175 \end{array}$  Page 25

Val Tyr Phe Ser Leu Leu Leu Ile Gln Leu Val Leu Ser Cys Phe Ser Asp Arg Ser Pro Leu Phe Ser Glu Thr Ile His Asp Pro Asn Pro Cys Pro Glu Ser Ser Ala Ser Phe Leu Ser Arg Ile Thr Phe Trp Trp Ile 210 215 220 Thr Gly Leu Ile Val Arg Gly Tyr Arg Gln Pro Leu Glu Gly Ser Asp Leu Trp Ser Leu Asn Lys Glu Asp Thr Ser Glu Gln Val Val Pro Val Leu Val Lys Asn Trp Lys Lys Glu Cys Ala Lys Thr Arg Lys Gln Pro Val Lys Val Val Tyr Ser Ser Lys Asp Pro Ala Gln Pro Lys Glu Ser 275 280 285 Ser Lys Val Asp Ala Asn Glu Glu Val Glu Ala Leu Ile Val Lys Ser 290 295 300 Pro Gln Lys Glu Trp Asn Pro Ser Leu Phe Lys Val Leu Tyr Lys Thr 305 310 315 320 Phe Gly Pro Tyr Phe Leu Met Ser Phe Phe Phe Lys Ala Ile His Asp Leu Met Met Phe Ser Gly Pro Gln Ile Leu Lys Leu Leu Ile Lys Phe Val Asn Asp Thr Lys Ala Pro Asp Trp Gln Gly Tyr Phe Tyr Thr Val Leu Leu Phe Val Thr Ala Cys Leu Gln Thr Leu Val Leu His Gln Tyr Phe His Ile Cys Phe Val Ser Gly Met Arg Ile Lys Thr Ala Val Ile 385 390 395 400 Gly Ala Val Tyr Arg Lys Ala Leu Val Ile Thr Asn Ser Ala Arg Lys 405 410 415 Ser Ser Thr Val Gly Glu Ile Val Asn Leu Met Ser Val Asp Ala Gln Page 26

Arg Phe Met Asp Leu Ala Thr Tyr Ile Asn Met Ile Trp Ser Ala Pro 445 445 Leu Gln Val Ile Leu Ala Leu Tyr Leu Leu Trp Leu Asn Leu Gly Pro 450 450 460 Ser Val Leu Ala Gly Val Ala Val Met Val Leu Met Val Pro Val Asn 465 470 480 Ala Val Met Ala Met Lys Thr Lys Thr Tyr Gln Val Ala His Met Lys 485 490 495 Ser Lys Asp Asn Arg Ile Lys Leu Met Asn Glu Ile Leu Asn Gly Ile 500 505 510 Lys Val Leu Lys Leu Tyr Ala Trp Glu Leu Ala Phe Lys Asp Lys Val 515 520 525 Leu Ala Ile Arg Gln Glu Glu Leu Lys Val Leu Lys Lys Ser Ala Tyr 530 535 Leu Ser Ala val Gly Thr Phe Thr Trp Val Cys Thr Pro Phe Leu val 545 550 555 560 Ala Leu Cys Thr Phe Ala Val Tyr Val Thr Ile Asp Glu Asn Asn Ile 565 575 Leu Asp Ala Gln Thr Ala Phe Val Ser Leu Ala Leu Phe Asn Ile Leu 580 590 Arg Phe Pro Leu Asn Ile Leu Pro Met Val Ile Ser Ser Ile Val Gln 595 600 605 Ala Ser Val Ser Leu Lys Arg Leu Arg Ile Phe Leu Ser His Glu Glu 610 620 Leu Glu Pro Asp Ser Ile Glu Arg Arg Pro Val Lys Asp Gly Gly Gly 635 635 640 Thr Asn Ser Ile Thr Val Arg Asn Ala Thr Phe Thr Trp Ala Arg Ser 645 650 655 Asp Pro Pro Thr Leu Asn Gly Ile Thr Phe Ser Ile Pro Glu Gly Ala 660 665 670

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Leu Val Ala Val Val Gly Gln Val Gly Cys Gly Lys Ser Ser Leu Leu
675 680 685 Ser Ala Leu Leu Ala Glu Met Asp Lys Val Glu Gly His Val Ala Ile 690 695 700 Lys Gly Ser Val Ala Tyr Val Pro Gln Gln Ala Trp Ile Gln Asn Asp Ser Leu Arg Glu Asn Ile Leu Phe Gly Cys Gln Leu Glu Glu Pro Tyr Tyr Arg Ser Val Ile Gln Ala Cys Ala Leu Leu Pro Asp Leu Glu Ile 740 750 Leu Pro Ser Gly Asp Arg Thr Glu Ile Gly Glu Lys Gly Val Asn Leu
755 760 765 Ser Gly Gly Gln Lys Gln Arg Val Ser Leu Ala Arg Ala Val Tyr Ser Asn Ala Asp Ile Tyr Leu Phe Asp Asp Pro Leu Ser Ala Val Asp Ala 785 790 795 800 His Val Gly Lys His Ile Phe Glu Asn Val Ile Gly Pro Lys Gly Met 805 810 815 Leu Lys Asn Lys Thr Arg Ile Leu Val Thr His Ser Met Ser Tyr Leu Pro Gln Val Asp Val Ile Ile Val Met Ser Gly Gly Lys Ile Ser Glu 835 840 845 Met Gly Ser Tyr Gln Glu Leu Leu Ala Arg Asp Gly Ala Phe Ala Glu 850 855 860 Phe Leu Arg Thr Tyr Ala Ser Thr Glu Gln Glu Gln Asp Ala Glu Glu 865 870 875 880 Asn Gly Val Thr Gly Val Ser Gly Pro Gly Lys Glu Ala Lys Gln Met Glu Asn Gly Met Leu Val Thr Asp Ser Ala Gly Lys Gln Leu Gln Arg 900 905 910 Gln Leu Ser Ser Ser Ser Tyr Ser Gly Asp Ile Ser Arg His His

Asn Ser Thr Ala Glu Leu Gln Lys Ala Glu Ala Lys Lys Glu Glu Thr 930 940 Trp Lys Leu Met Glu Ala Asp Lys Ala Gln Thr Gly Gln Val Lys Leu 945 950 955 960 Ser Val Tyr Trp Asp Tyr Met Lys Ala Ile Gly Leu Phe Ile Ser Phe 965 970 Leu Ser Ile Phe Leu Phe Met Cys Asn His Val Ser Ala Leu Ala Ser 980 985 990 Asn Tyr Trp Leu Ser Leu Trp Thr Asp Asp Pro Ile Val Asn Gly Thr 995 1000 1005 Gln Glu His Thr Lys Val Arg Leu Ser Val Tyr Gly Ala Leu Gly 1010 1020 ile Ser Gln Gly ile Ala Val Phe Gly Tyr Ser Met Ala Val Ser 1025 1030 1035 Ile Gly Gly Ile Leu Ala Ser Arg Cys Leu His Val Asp Leu Leu 1040 1050 His Ser Ile Leu Arg Ser Pro Met Ser Phe Phe Glu Arg Thr Pro 1055 1060 1065 Ser Gly Asn Leu Val Asn Arg Phe Ser Lys Glu Leu Asp Thr Val 1070 1080 Asp Ser Met Ile Pro Glu Val 1085 Met Phe Met Gly Ser Leu 1090 1095Phe Asn Val Ile Gly Ala Cys Ile Val Ile Leu Leu Ala Thr Pro 1100 1110 Ile Ala Ala Ile Ile Ile Pro Pro Leu Gly Leu Ile Tyr Phe Phe 1115 1120 1125 Val Gln Arg Phe Tyr Val Ala Ser Ser Arg Gln Leu Lys Arg Leu 1130 1140 Glu Ser Val Ser Arg Ser Pro Val Tyr Ser His Phe Asn Glu Thr 1145 1150 1155 Leu Leu Gly Val Ser Val Ile Arg Ala Phe Glu Glu Gln Glu Arg

Phe Ile His Gln Ser Asp Leu Lys Val Asp Glu Asn Gln Lys Ala 1175 1180 1185 Tyr Tyr Pro Ser Ile Val Ala Asn Arg Trp Leu Ala Val Arg Leu 1190 1200 Glu Cys Val Gly Asn Cys Ile Val Leu Phe Ala Ala Leu Phe Ala 1205 1210 1215 val Ile Ser Arg His Ser Leu Ser Ala Gly Leu val Gly Leu Ser 1220 1230 Val Ser Tyr Ser Leu Gln Val Thr Thr Tyr Leu Asn Trp Leu Val 1235 1240 1245 Arg Met Ser Ser Glu Met Glu Thr Asn Ile Val Ala Val Glu Arg 1250 Leu Lys Glu Tyr Ser Glu Thr Glu Lys Glu Ala Pro Trp Gln Ile 1265 1270 1275 Gln Glu Thr Ala Pro Pro Ser Ser Trp Pro Gln Val Gly Arg Val 1280 1285 1290 Glu Phe Arg Asn Tyr Cys Leu Arg Tyr Arg Glu Asp Leu Asp Phe 1295 1300 Val Leu Arg His Ile Asn Val Thr Ile Asn Gly Gly Glu Lys Val 1310 1320 Gly Ile val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Thr Leu 1325 1330 1335 Gly Leu Phe Arg Ile Asn Glu Ser Ala Glu Gly Glu Ile Ile 1340 1350 Asp Gly Ile Asn Ile Ala Lys Ile Gly Leu His Asp Leu Arg Phe 1365 1366 Lys Ile Thr Ile Ile Pro Gln  $% \left( 1370\right) =1370$  Thr Ile Ile Pro Gln Asp Pro Val Leu Phe 380 Ser Gly Ser 1380Leu Arg Met Asn Leu Asp Pro Phe Ser Gln Tyr Ser Asp Glu Glu 1385 1390 1395 Val Trp Thr Ser Leu Glu Leu Ala His Leu Lys Asp Phe Val Ser Page 30

Ala Leu Pro Asp Lys Leu Asp His Glu Cys Ala Glu Gly Gly Glu 1415 1425 1425 Asn Leu Ser Val Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala 1435 1440 Leu Leu Arg Lys Thr Lys Ile Leu Val Leu Asp Glu Ala Thr Ala 1445 1455 Ala Val Asp Leu Glu Thr Asp Asp Leu Ile Gln Ser Thr Ile Arg 1460 1470 Thr Gln Phe Glu Asp Cys Thr Val Leu Thr Ile Ala His Arg Leu 1475 1480 1485 Asn Thr Ile Met Asp Tyr Thr Arg Val Ile Val Leu Asp Lys Gly 1490 1500 Glu Ile Gln Glu Tyr Gly Ala Pro Ser Asp Leu Leu Gln Gln Arg 1505 1510 Gly Leu Phe Tyr Ser Met Ala Lys Asp Ala Gly Leu Val Gly Gly 1520 1530 Gly Gly Gly Met Leu Ser Arg Lys Gly Ile Ile Pro Glu Glu 1535 1540 1545 Tyr Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr 1550 1560  $\mbox{Arg Thr}$   $\mbox{Arg Glu}$   $\mbox{Arg Arg}$   $\mbox{Ala}$   $\mbox{Arg Phe Val Ser}$   $\mbox{Lys}$   $\mbox{Lys}$  Gly  $\mbox{Asn}$   $\mbox{1575}$ Cys Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu 1580 1590 Gln Asp Val Phe Thr Thr Leu Val Asp Leu Lys Trp Pro His Thr 1595 1600 1605 Leu Leu Ile Phe Thr Met Ser Phe Leu Cys Ser Trp Leu Leu Phe 1610

Ala Met Val Trp Trp Leu Ile Ala Phe Ala His Gly Asp Leu Ala 1625 1630 1635

### Pro Gly Glu Gly Thr Asn Val Pro Cys Val Thr Ser Ile His Ser 1640 1645

Phe Ser Ser Ala Phe Leu Phe Ser Ile Glu Val Gln Val Thr Ile 1655

Gly Phe Gly Gly Arg Met Val Thr Glu Glu Cys Pro Leu Ala Ile 1670 1680

Leu Ile Leu Ile Val Gln Asn Ile Val Gly Leu Met Ile Asn Ala 1685 1690 1695

Ile Met Leu Gly Cys Ile Phe Met Lys Thr Ala Gln Ala His Arg 1700 1710 1710

Arg Ala Glu Thr Leu Ile Phe Ser Lys His Ala Val Ile Thr Leu 1715 1720 1725

Arg His Gly Arg Leu Cys Phe Met Leu Arg Val Gly Asp Leu Arg 1730 1740

Lys Ser Met Ile Ile Ser Ala Thr Ile His Met Gln Val Val Arg

Lys Thr Thr Ser Pro Glu Gly Glu Val Val Pro Leu His Gln Val 1760 1770

ASP Ile Pro Met Glu ASR Gly Val Gly Gly ASR Gly Ile Phe Leu 1775 1780

Val Ala Pro Leu Ile Ile Tyr His Val Ile Asp Ser Asn Ser Pro 1790 1800

Leu Tyr Asp Leu Ala Pro Ser Asp Leu His His Gln Asp Leu 1805 1810 1815

Glu Ile Ile Val Ile Leu Glu Gly Val Val Glu Thr Thr Gly Ile  $1820 \\ \hspace*{1.5cm} 1825 \\ \hspace*{1.5cm} 1830 \\ \hspace*{1.5cm}$ 

Thr Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp Glu Ile Leu Trp 1835 1840 1845

Gly Gln Arg Phe Val Pro Ile Val Ala Glu Glu Asp Gly Arg Tyr 1850 1860

Ser Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile Lys Val Pro Thr 1865 1870 1875

Pro Leu Cys Thr Ala Arg Gln Leu Asp Glu Asp Arg Ser 1880 1885

<210> 5 <211> 1875

<213> Saccharomyces cerevisiae

<400>

Met Ala Gly Asn Leu Val Ser Trp Ala Cys Lys Leu Cys Arg Ser Pro

ile Asp Gly Val ile Leu Asn Leu Ser Ala ile Phe Met ile Thr Phe 35 45

Gly Ile Arg Asp Leu Val Asn Leu Cys Lys Lys His Ser Gly Ile 50 60

Lys Tyr Arg Arg Asn Trp Ile Ile Val Ser Arg Met Ala Leu Val Leu 65  $^{75}$ 

Leu Glu Ile Ala Phe Val Ser Leu Ala Ser Leu Asn Ile Ser Lys Glu 85 95

Glu Ala Glu Asn Phe Thr Ile Val Ser Gln Tyr Ala Ser Thr Met Leu 105 110

Ser Leu Phe Val Ala Leu Ala Leu His Trp Ile Glu Tyr Asp Arg Ser 125 125

Val Val Ala Asn Thr Val Leu Leu Phe Tyr Trp Leu Phe Glu Thr Phe 130 140

Gly Asn Phe Ala Lys Leu Ile Asn Ile Leu Ile Arg His Thr Tyr Glu 145 155 160

Gly Ile Trp Tyr Ser Gly Gln Thr Gly Phe Ile Leu Thr Leu Phe Gln 175 175

Val Ile Thr Cys Ala Ser Ile Leu Leu Leu Glu Ala Leu Pro Lys Lys 180 190

Pro Leu Met Pro His Gln His Ile His Gln Thr Leu Thr Arg Arg Lys  $195 \ \ \, 200 \ \ \,$ 

Pro Asn Pro Tyr Asp Ser Ala Asn Ile Phe Ser Arg Ile Thr Phe Ser 210 215 220 Trp Met Ser Gly Leu Met Lys Thr Gly Tyr Glu Lys Tyr Leu Val Glu 225 230 235 240 Ala Asp Leu Tyr Lys Leu Pro Arg Asn Phe Ser Ser Glu Glu Leu Ser Gln Lys Leu Glu Lys Asn Trp Glu Asn Glu Leu Lys Gln Lys Ser Asn 260 265 270 Pro Ser Leu Ser Trp Ala Ile Cys Arg Thr Phe Gly Ser Lys Met Leu Leu Ala Ala Phe Phe Lys Ala Ile His Asp Val Leu Ala Phe Thr Gln 290 300Pro Gln Leu Leu Arg Ile Leu Ile Lys Phe Val Thr Asp Tyr Asn Ser 305 310 315 320 Glu Arg Gln Asp Asp His Ser Ser Leu Gln Gly Phe Glu Asn Asn His Pro Gln Lys Leu Pro Ile Val Arg Gly Phe Leu Ile Ala Phe Ala Met Phe Leu Val Gly Phe Thr Gln Thr Ser Val Leu His Gln Tyr Phe Leu 355 360 365 ASN Val Phe Asn Thr Gly Met Tyr Ile Lys Ser Ala Leu Thr Ala Leu 370 375 380 Ile Tyr Gln Lys Ser Leu Val Leu Ser Asn Glu Ala Ser Gly Leu Ser Ser Thr Gly Asp Ile Val Asn Leu Met Ser Val Asp Val Gln Lys Leu Gln Asp Leu Thr Gln Trp Leu Asn Leu Ile Trp Ser Gly Pro Phe Gln
420 425 430 Ile Ile Ile Cys Leu Tyr Ser Leu Tyr Lys Leu Leu Gly Asn Ser Met 435 440 445 Trp Val Gly Val Ile Ile Leu Val Ile Met Met Pro Leu Asn Ser Phe 450 460 Page 34

Leu Met Arg Ile Gln Lys Lys Leu Gln Lys Ser Gln Met Lys Tyr Lys 455 470 480 Asp Glu Arg Thr Arg val Ile Ser Glu Ile Leu Asn Asn Ile Lys Ser 495 495 Leu Lys Leu Tyr Ala Trp Glu Lys Pro Tyr Arg Glu Lys Leu Glu Glu 500 510 Val Arg Asn Asn Lys Glu Leu Lys Asn Leu Thr Lys Leu Gly Cys Tyr 520 Met Ala val Thr Ser Phe Gln Phe Asn Ile Val Pro Phe Leu Val Ser 530 540 Cys Cys Thr Phe Ala val Phe Val Tyr Thr Glu Asp Arg Ala Leu Thr 545 555 560 Thr Asp Leu val Phe Pro Ala Leu Thr Leu Phe Asn Leu Leu Ser Phe 570 575 Pro Leu Met Ile Ile Pro Met Val Leu Asn Ser Phe Ile Glu Ala Ser 580 585Val Ser Ile Gly Arg Leu Phe Thr Phe Phe Thr Asn Glu Glu Leu Gln 595 600 605 Pro Asp Ser val Gln Arg Leu Pro Lys Val Lys Asn Ile Gly Asp val 610 620 Ala Ile Asn Ile Gly Asp Asp Ala Thr Phe Leu Trp Gln Arg Lys Pro 625 630 640 Glu Tyr Lys val Ala Leu Lys Asn Ile Asn Phe Gln Ala Lys Lys Gly 645 650 Asn Leu Thr Cys Ile val Gly Lys val Gly Ser Gly Lys Thr Ala Leu 660 665 670 Leu Ser Cys Met Leu Gly Asp Arg Phe Arg Val Lys Gly Phe Ala Thr 675 685 Val His Gly Ser val Ala Tyr val Ser Gln val Pro Trp Ile Met Asn 690 700 Gly Thr val Lys Glu Asn Ile Leu Phe Gly His Arg Tyr Asp Ala Glu Page 35

Phe Tyr Glu Lys Thr Ile Lys Ala Cys Ala Leu Thr Ile Asp Leu Ala Ile Leu Met Asp Gly Asp Lys Thr Leu Val Gly Glu Lys Gly Ile Ser Leu Ser Gly Gly Gln Lys Ala Arg Leu Ser Leu Ala Arg Ala Val Tyr Ala Arg Ala Asp Thr Tyr Leu Leu Asp Asp Pro Leu Ala Ala Val Asp Glu His Val Ala Arg His Leu Ile Glu His Val Leu Gly Pro Asn Gly 785 790 795 800 Leu Leu His Thr Lys Thr Lys Val Leu Ala Thr Asn Lys Val Ser Ala Leu Ser Ile Ala Asp Ser Ile Ala Leu Leu Asp Asn Gly Glu Ile Thr 820 825 Gln Gln Gly Thr Tyr Asp Glu Ile Thr Lys Asp Ala Asp Ser Pro Leu 835 840 845 Trp Lys Leu Leu Asn Asn Tyr Gly Lys Lys Asn Asn Gly Lys Ser Asn 850 855 860 Glu Phe Gly Asp Ser Ser Glu Ser Ser Val Arg Glu Ser Ser Ile Pro 865 870 875 880 Val Glu Gly Glu Leu Glu Gln Leu Gln Lys Leu Asn Asp Leu Asp Phe Gly Asn Ser Asp Ala Ile Ser Leu Arg Arg Ala Ser Asp Ala Thr Leu Gly Ser Ile Asp Phe Gly Asp Asp Glu Asn Ile Ala Lys Arg Glu His Arg Glu Gln Gly Lys Val Lys Trp Asn Ile Tyr Leu Glu Tyr Ala Lys Ala Cys Asn Pro Lys Ser Val Cys Val Phe Ile Leu Phe Ile Val Ile

# \$ s263US104.ST25 Ser Met Phe Leu Ser Val Met Gly Asn Val Trp Leu Lys His Trp Ser 965 970 975Glu Val Asn Ser Arg Tyr Gly Ser Asn Pro Asn Ala Ala Arg Tyr Leu 980 985 990 Ala Ile Tyr Phe Ala Leu Gly Ile Gly Ser Ala Leu Ala Thr Leu Ile Gln Thr Ile Val Leu Trp Val Phe Cys Thr Ile His Ala Ser Lys Tyr Leu His Asn Leu Met Thr Asn Ser Val Leu Arg Ala Pro Met Thr Phe Phe Glu Thr Thr Pro Ile Gly Arg Ile Leu Asn Arg Phe 1040 1045 1050 Ser Asn Asp Ile Tyr Lys Val Asp Ala Leu Leu Gly Arg Thr Phe Ser Gln Phe Phe Val Asn Ala Val Lys Val Thr Phe Thr Ile Thr 1070 1080 Val Ile Cys Ala Thr Thr Trp Gln Phe Ile Phe Ile Ile Ile Pro Leu Ser Val Phe Tyr Ile Tyr Tyr Gln Gln Tyr Tyr Leu Arg Thr Ser Arg Glu Leu Arg Arg Leu Asp Ser Ile Thr Arg Ser Pro Ile 1115 1120 1125 Tyr Ser His Phe Gln Glu Thr Leu Gly Gly Leu Ala Thr Val Arg 1130 1140 Gly Tyr Ser Gln Gln Lys Arg Phe Ser His Ile Asn Gln Cys Arg Ile Asp Asn Asn Met Ser Ala Phe Tyr Pro Ser Ile Asn Ala Asn Arg Trp Leu Ala Tyr Arg Leu Glu Leu Ile Gly Ser Ile Ile 1175 1180 1185

Leu Gly Ala Ala Thr Leu Ser Val Phe Arg Leu Lys Gln Gly Thr

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Leu	Thr 1205	Ala	Gly	Met	∨a1	Gly 1210	Leu	Ser	Leu	Ser	Tyr 1215	Ala	Leu	Gln
Ile	Thr 1220	Gln	Thr	Leu	Asn	Trp 1225	Ile	val	Arg	Met	Thr 1230	val	Glu	val
Glu	Thr 1235	Asn	Ile	٧a٦	ser	Val 1240	G1u	Arg	Ile	Lys	Glu 1245	туг	Ala	Asp
Leu	Lys 1250	Ser	Glu	Аlа	Pro	Leu 1255	Ile	val	Glu	Gly	ніs 1260	Arg	Pro	Pro
Lys	Glu 1265	Trp	Pro	Ser	Gln	Gly 1270	Asp	Ile	Lys	Phe	Asn 1275	Asn	Tyr	Ser
Thr	Arg 1280	туг	Arg	Pro	Glu	Leu 1285	Asp	Leu	val	Leu	Lys 1290	His	Ile	Asn
Ile	ніs 1295	Ile	Lys	Pro	Asn	Glu 1300	Lys	Val	Gly	Ile	Val 1305	Gly	Arg	Thr
Gly	Ala 1310	Gly	Lys	Ser	Ser	Leu 1315	Thr	Leu	Ala	Leu	Phe 1320	Arg	Met	Ile
Glu	Ala 1325	Ser	Glu	Gly	Asn	Ile 1330	٧a٦	Ile	Asp	Asn	Ile 1335	Аlа	IJe	Asn
Glu	Ile 1340	Glу	Leu	Tyr	Asp	Leu 1345	Arg	His	Lys	Leu	Ser 1350	Ile	Ile	Pro
Gln	Asp 1355	Ser	Gln	۷a٦	Phe	G]u 1360	G]y	Thr	val	Arg	G]u 1365	Asn	Ile	Asp
Pro	Ile 1370	Asn	Gln	Tyr	Thr	Asp 1375	Glu	Ala	Ile	Trp	Arg 1380	Ala	Leu	Glu
Leu	Ser 1385	His	Leu	Lys	Glu	ніs 1390	val	Leu	ser	Met	Ser 1395	Asn	Asp	GÌу
Leu	Asp 1400	Ala	Gln	Leu	Thr	Glu 1405	G1y	Glу	Gly	Asn	Leu 1410	Ser	Val	Gly
Gln	Arg 1415	Gln	Leu	Leu	Cys	Leu 1420	Аlа	Arg	Ala	Met	Leu 1425	val	Pro	Ser
Lys	Ile 1430	Leu	Val	Leu	Asp	Glu 1435	Ala	Thr		А1а е 38	1440	Asp	Val	Glu

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Thr Asp Lys Val Val Gln Glu Thr Ile Arg Thr Ala Phe Lys Asp 1445 1450 1455 Arg Thr Ile Leu Thr Ile Ala His Arg Leu Asn Thr Ile Met Asp 1460 1470 Ser Asp Arg Ile Ile Val Leu Asp Asn Gly Lys Val Ala Glu Phe 1485 1485 ASP Ser Pro Gly Gln Leu Leu Ser ASP ASn Lys Ser Leu Phe Tyr 1490 Ser Leu Cys Met Glu Ala Gly Leu Val Asn Glu Asn Gly Gly Gly 1505 1510 1515 Gly Gly Met Leu Ser Arg Lys Gly Ile Ile Pro Glu Glu Tyr 1520 1530 Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr Arg 1535 1545 Thr Arg  $_{1550}^{}$  Glu Arg Arg Ala Arg  $_{1555}^{}$  Phe Val Ser Lys  $_{1560}^{}$  Gly Asn Cys Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu Gln 1565 1570 1575 ASP Val Phe Thr Thr Leu Val ASP Leu Lys Trp Pro His Thr Leu 1580 1590 Leu Ile Phe Thr Met Ser Phe Leu Cys Ser Trp Leu Leu Phe Ala 1595 Met Val Trp Trp Leu Ile Ala Phe Ala His Gly Asp Leu Ala Pro 1610 1620 Gly Glu Gly Thr Asn Val Pro Cys Val Thr Ser Ile His Ser Phe 1625 1630 1635 Ser Ser Ala Phe Leu Phe Ser Ile Glu Val Gln Val Thr Ile Gly 1640 1650 Phe Gly Gly Arg Met Val Thr Glu Glu Cys Pro Leu Ala Ile Leu 1665 1665 Ile Leu Ile Val Gln Asn Ile Val Gly Leu Met Ile Asn Ala Ile

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Met Leu Gly Cys Ile Phe Met Lys Thr Ala Gln Ala His Arg Arg 1685 1690 1695 Ala Glu Thr Leu Ile Phe Ser Lys His Ala Val Ile Thr Leu Arg His Gly Arg Leu Cys Phe Met Leu Arg Val Gly Asp Leu Arg Lys 1715 1720 1725 Ser Met Ile Ile Ser Ala Thr Ile His Met Gln Val Val Arg Lys 1730 1735 1740 Thr Thr Ser Pro Glu Gly Glu Val Val Pro Leu His Gln Val Asp 1745 1750 1755 Ile Pro Met Glu Asn Gly Val Gly Gly Asn Gly Ile Phe Leu Val Ala Pro Leu Ile Ile Tyr His Val Ile Asp Ser Asn Ser Pro Leu 1775 1780 1785 Tyr Asp Leu Ala Pro Ser Asp Leu His His His Gln Asp Leu Glu Ile Ile Val Ile Leu Glu Gly Val Val Glu Thr Thr Gly Ile Thr 1805 1810 1815 Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp Glu Ile Leu Trp Gly 1820 1825 1830 Gln Arg Phe Val Pro Ile Val Ala Glu Glu Asp Gly Arg Tyr Ser Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile Lys Val Pro Thr Pro 1850 1860

<400> 6

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Leu Cys Thr Ala Arg Gln Leu Asp Glu Asp Arg Ser 1865 1870 1875

<sup>&</sup>lt;210> 6 <211> 1927 <212> PRT <213> Homo sapiens

1

Asp Trp Asn Val Thr Trp Asn Thr Ser Asn Pro Asp Phe Thr Lys Cys Phe Gln Asn Thr Val Leu Val Trp Val Pro Cys Phe Tyr Leu Trp Ala Cys Phe Pro Phe Tyr Phe Leu Tyr Leu Ser Arg His Asp Arg Gly Tyr Ile Gln Met Thr Pro Leu Asn Lys Thr Lys Thr Ala Leu Gly Phe Leu Leu Trp Ile Val Cys Trp Ala Asp Leu Phe Tyr Ser Phe Trp Glu Arg Ser Arg Gly Ile Phe Leu Ala Pro Val Phe Leu Val Ser Pro Thr Leu Leu Gly Ile Thr Thr Leu Leu Ala Thr Phe Leu Ile Gln Leu Glu Arg 115 120 125 Arg Lys Gly Val Gln Ser Ser Gly Ile Met Leu Thr Phe Trp Leu Val Ala Leu Val Cys Ala Leu Ala Ile Leu Arg Ser Lys Ile Met Thr Ala 145 150 155 160 Leu Lys Glu Asp Ala Gln Val Asp Leu Phe Arg Asp Ile Thr Phe Tyr 165 170 175 Val Tyr Phe Ser Leu Leu Leu Ile Gln Leu Val Leu Ser Cys Phe Ser 180 185 190 Asp Arg Ser Pro Leu Phe Ser Glu Thr Ile His Asp Pro Asn Pro Cys 195 200 205 Pro Glu Ser Ser Ala Ser Phe Leu Ser Arg Ile Thr Phe Trp Trp Ile Thr Gly Leu Ile Val Arg Gly Tyr Arg Gln Pro Leu Glu Gly Ser Asp Leu Trp Ser Leu Asn Lys Glu Asp Thr Ser Glu Gln Val Val Pro Val 245 255

s263US104.ST25 Leu Val Lys Asn Trp Lys Lys Glu Cys Ala Lys Thr Arg Lys Gln Pro 260 265 270 Val Lys Val Val Tyr Ser Ser Lys Asp Pro Ala Gln Pro Lys Glu Ser 275 280 285 Ser Lys Val Asp Ala Asp Glu Glu Val Glu Ala Leu Ile Val Lys Ser Pro Gln Lys Glu Trp Asn Pro Ser Leu Phe Lys Val Leu Tyr Lys Thr 315 310 315Phe Gly Pro Tyr Phe Leu Met Ser Phe Phe Phe Lys Ala Ile His Asp 325 330 335 Leu Met Met Phe Ser Gly Pro Gln Ile Leu Lys Leu Leu Ile Lys Phe Val Asn Asp Thr Lys Ala Pro Asp Trp Gln Gly Tyr Phe Tyr Thr Val Leu Leu Phe Val Thr Ala Cys Leu Gln Thr Leu Val Leu His Gln Tyr 370 375 380 Phe His Ile Cys Phe Val Ser Gly Met Arg Ile Lys Thr Ala Val Ile 385 390 395 400 Gly Ala Val Tyr Arg Lys Ala Leu Val Ile Thr Asn Ser Ala Arg Lys
405 410 415 Ser Ser Thr Val Gly Glu Ile Val Asn Leu Met Ser Val Asp Ala Gln
420 425 430 Arg Phe Met Asp Leu Ala Thr Tyr Ile Asn Met Ile Trp Ser Ala Pro
435 440 445 Leu Gln Val Ile Leu Ala Leu Tyr Leu Leu Trp Leu Asn Leu Gly Pro Ser Val Leu Ala Gly Val Ala Val Met Val Leu Met Val Pro Val Asn 465 470 475 480 Ala Val Met Ala Met Lys Thr Lys Thr Tyr Gln Val Ala His Met Lys 485 490 495 Ser Lys Asp Asn Arg Ile Lys Leu Met Asn Glu Ile Leu Asn Gly Ile 500 505 510

### s263uS104.ST25

Lys Val Leu Lys Leu Tyr Ala Trp Glu Leu Ala Phe Lys Asp Lys Val Leu Ala Ile Arg Gln Glu Glu Leu Lys Val Leu Lys Lys Ser Ala Tyr Leu Ser Ala Val Gly Thr Phe Thr Trp Val Cys Thr Pro Phe Leu Val Ala Leu Cys Thr Phe Ala Val Tyr Val Thr Ile Asp Glu Asn Asn Ile 565 570 575 Leu Asp Ala Gln Thr Ala Phe Val Ser Leu Ala Leu Phe Asn Ile Leu Arg Phe Pro Leu Asn Ile Leu Pro Met Val Ile Ser Ser Ile Val Gln 595 600 605 Ala Ser Val Ser Leu Lys Arg Leu Arg Ile Phe Leu Ser His Glu Glu 610 620 Leu Glu Pro Asp Ser Ile Glu Arg Arg Pro Val Lys Asp Gly Gly Gly 625 630 635 640 Thr Asn Ser Ile Thr Val Arg Asn Ala Thr Phe Thr Trp Ala Arg Ser Asp Pro Pro Thr Leu Asn Gly Ile Thr Phe Ser Ile Pro Glu Gly Ala 660 670 Leu Val Ala Val Val Gly Gln Val Gly Cys Gly Lys Ser Ser Leu Leu 675 680 685 Ser Ala Leu Leu Ala Glu Met Asp Lys Val Glu Gly His Val Ala Ile 690 695 700 Lys Gly Ser Val Ala Tyr Val Pro Gln Gln Ala Trp Ile Gln Asn Asp Ser Leu Arg Glu Asn Ile Leu Phe Gly Cys Gln Leu Glu Glu Pro Tyr Tyr Arg Ser Val Ile Gln Ala Cys Ala Leu Leu Pro Asp Leu Glu Ile 740 745 750 Leu Pro Ser Gly Asp Arg Thr Glu Ile Gly Glu Lys Gly Val Asn Leu 755 760 765

### s263us104.ST25

Ser Gly Gly Gln Lys Gln Arg Val Ser Leu Ala Arg Ala Val Tyr Ser Asn Ala Asp Ile Tyr Leu Phe Asp Asp Pro Leu Ser Ala Val Asp Ala 785 790 795 800 His Val Gly Lys His Ile Phe Glu Asn Val Ile Gly Pro Lys Gly Met Leu Lys Asn Lys Thr Arg Ile Leu Val Thr His Ser Met Ser Tyr Leu 820 825 830 Pro Gln Val Asp Val Ile Ile Val Met Ser Gly Gly Lys Ile Ser Glu 835 840 845 Met Gly Ser Tyr Gln Glu Leu Leu Ala Arg Asp Gly Ala Phe Ala Glu 850 855 860 Phe Leu Arg Thr Tyr Ala Ser Thr Glu Gln Glu Gln Asp Ala Glu Glu 865 870 875 880 Asn Gly Val Thr Gly Val Ser Gly Pro Gly Lys Glu Ala Lys Gln Met Glu Asn Gly Met Leu Val Thr Asp Ser Ala Gly Lys Gln Leu Gln Arg Gln Leu Ser Ser Ser Ser Ser Tyr Ser Gly Asp Ile Ser Arg His His 915 920 925 Asn Ser Thr Ala Glu Leu Gln Lys Ala Glu Ala Lys Lys Glu Glu Thr Trp Lys Leu Met Glu Ala Asp Lys Ala Gln Thr Gly Gln Val Lys Leu 945 950 955 960 Ser Val Tyr Trp Asp Tyr Met Lys Ala Ile Gly Leu Phe Ile Ser Phe Leu Ser Ile Phe Leu Phe Met Cys Asn His Val Ser Ala Leu Ala Ser Asn Tyr Trp Leu Ser Leu Trp Thr Asp Asp Pro Ile Val Asn Gly Thr Gln Glu His Thr Lys Val Arg Leu Ser Val Tyr Gly Ala Leu Gly Page 44

Ile Ser Gln Gly Ile Ala Val Phe Gly Tyr Ser Met Ala Val Ser 1025 1030 1035 Ile Gly Gly Ile Leu Ala Ser Arg Cys Leu His Val Asp Leu Leu 1040 1045 1050 His Ser Ile Leu Arg Ser Pro Met Ser Phe Phe Glu Arg Thr Pro 1055 1060 1065 Ser Gly Asn Leu Val Asn Arg Phe Ser Lys Glu Leu Asp Thr Val Asp Ser Met Ile Pro Glu Val Ile Lys Met Phe Met Gly Ser Leu 1085 1090 1095 Phe Asn Val Ile Gly Ala Cys Ile Val Ile Leu Leu Ala Thr Pro 1100 1105 1110 Ile Ala Ala Ile Ile Ile Pro Pro Leu Gly Leu Ile Tyr Phe Phe 1115 1120 1125 Val Gln Arg Phe Tyr Val Ala Ser Ser Arg Gln Leu Lys Arg Leu 1130 1140 Glu Ser Val Ser Arg Ser Pro Val Tyr Ser His Phe Asn Glu Thr Leu Leu Gly Val Ser Val Ile Arg Ala Phe Glu Glu Gln Glu Arg 1160 1170 Phe Ile His Gln Ser Asp Leu Lys Val Asp Glu Asn Gln Lys Ala 1175 1180 1185 Tyr Tyr Pro Ser Ile Val Ala Asn Arg Trp Leu Ala Val Arg Leu 1190 1200 Glu Cys Val Gly Asn Cys Ile Val Leu Phe Ala Ala Leu Phe Ala 1205 1210 1215 Val Ile Ser Arg His Ser Leu Ser Ala Gly Leu Val Gly Leu Ser 1220 1230 Val Ser Tyr Ser Leu Gln Val Thr Thr Tyr Leu Asn Trp Leu Val 1235 1240 1245

1015

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	\$26303104.3123													
Asn	Thr 1490	Ile	Met	Asp	Tyr	Thr 1495	Arg	٧a٦	Ile	٧a٦	Leu 1500	Asp	Lys	Gly
Glu	11e 1505	Gln	Glu	Tyr	Gly	Ala 1510	Pro	Ser	Asp	Leu	Leu 1515	Gln	Gln	Arg
Gly	Leu 1520	Phe	туr	Ser	Met	Ala 1525	Lys	Asp	Αla	Glу	Leu 1530	val	Gly	Gly
Gly	Gly 1535	G٦y	GТу	Met	Leu	Ser 1540	Arg	Lys	Gly	Ile	Ile 1545	Pro	Glu	Glu
Tyr	∨a1 1550	Leu	Thr	Arg	Leu	Ala 1555	Glu	Asp	Pro	Аlа	Glu 1560	Pro	Arg	Tyr
Arg	Thr 1565	Arg	Glu	Arg	Arg	Ala 1570	Arg	Phe	٧a٦	Ser	Lys 1575	Lys	Gly	Asn
Cys	Asn 1580	val	Аlа	нis	Lys	Asn 1585	Ile	Arg	Glu	Gln	Gly 1590	Arg	Phe	Leu
Gln	Asp 1595	va1	Phe	Thr	Thr	Leu 1600	val	Asp	Leu	Lys	Trp 1605	Pro	нis	Thr
Leu	Leu 1610	Ile	Phe	Thr	Met	Ser 1615	Phe	Leu	Cys	Ser	Trp 1620	Leu	Leu	Phe
Ala	Met 1625	val	Trp	Тгр	Leu	Ile 1630	ΑΊа	Phe	Αla	нis	Gly 1635	Asp	Leu	Ala
Pro	Gly 1640	Glu	Glу	Thr	Asn	val 1645	Pro	Cys	val	Thr	Ser 1650	Ile	ніѕ	Ser
Phe	ser 1655	Ser	Ala	Phe	Leu	Phe 1660	Ser	Ile	Glu	val	Gln 1665	val	Thr	Ile
Gly	Phe 1670	Gly	Glу	Arg	Met	val 1675	Thr	Glu	Glu	Cys	Pro 1680	Leu	Αla	Ile
Leu	Ile 1685	Leu	Ile	٧a٦	Gln	Asn 1690	Ile	va1	Glу	Leu	меt 1695	Ile	Asn	Ala
Ile	Met 1700	Leu	Gly	Cys	Ile	Phe 1705	Met	Lys	Thr	Аlа	Gln 1710	Αla	ніѕ	Arg
Arg	Ala 1715	Glu	Thr	Leu	Ile	Phe 1720	Ser	Lys		А1а е 47	1725	Ile	Thr	Leu

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Arg His Gly Arg Leu Cys Phe Met Leu Arg Val Gly Asp Leu Arg Lys Ser Met Ile Ile Ser Ala Thr Ile His Met Gln Val Val Arg Lys Thr Thr Ser Pro Glu Gly Glu Val Val Pro Leu His Gln Val Asp Ile Pro Met Glu Asn Gly Val Gly Gly Asn Gly Ile Phe Leu Val Ala Pro Leu Ile Ile Tyr His Val Ile Asp Ser Asn Ser Pro 1790 1795 1800 Leu Tyr Asp Leu Ala Pro Ser Asp Leu His His Gln Asp Leu 1805 1810 1815 Glu Ile Ile Val Ile Leu Glu Gly Val Val Glu Thr Thr Gly Ile 1820 1830 Thr Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp Glu Ile Leu Trp 1835 1840 1845 Gly Gln Arg Phe Val Pro Ile Val Ala Glu Glu Asp Gly Arg Tyr 1850 1855 1860 Ser Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile Lys Val Pro Thr 1865 1870 1875 Pro Leu Cys Thr Ala Arg Gln Leu Asp Glu Asp Arg Ser Leu Leu 1880 1890 Asp Ala Leu Thr Leu Ala Ser Ser Arg Gly Pro Leu Arg Ala Ala Ser Val Ala Val Ala Lys Ala Lys Pro Lys Phe Ser Ile Ser Pro 1910 1915 1920

Asp Ser Leu Ser

<sup>&</sup>lt;210> 7 <211> 1961

<sup>&</sup>lt;212> PRT <213> Rattus rattus

<400> 7

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35 40 45 Trp Gly Ser Gln Ser Ser Lys val Gln Ile His His Asn Thr Trp Leu 50 60 His Phe Pro Gly His Asn Leu Arg Trp Ile Leu Thr Phe Ala Leu Leu 65 70 75 80 Phe Val His Val Cys Glu Ile Ala Glu Gly Ile Val Ser Asp Ser Gln Arg Ala Ser Arg His Leu His Leu Phe Met Pro Ala Val Met Gly Phe  $100 \\ 100 \\ 110$ Val Ala Thr Thr Thr Ser Ile Val Tyr Tyr His Asn Ile Glu Thr Ser 125 125 Asn Phe Pro Lys Leu Leu Leu Ala Leu Phe Leu Tyr Trp Val Met Ala 130 140 Phe Ile Thr Lys Thr Ile Lys Leu Val Lys Tyr Trp Gln Leu Gly Trp 145 155 160 Gly Met Ser Asp Leu Arg Phe Cys Ile Thr Gly Val Met Val Ile Leu 165 175 Asn Gly Leu Leu Met Ala Val Glu Ile Asn Val Ile Arg Val Arg Arg 180 180 190 Tyr Val Phe Phe Met Asn Pro Gln Lys Val Lys Pro Pro Glu Asp Leu 195 200 205 Gln Asp Leu Gly Val Arg Phe Leu Gln Pro Phe Val Asn Leu Leu Ser 210 215 220 Lys Ala Thr Tyr Trp Trp Met Asn Thr Leu Ile Ile Ser Ala His Arg 225 230 235 240 Lys Pro Ile Asp Leu Lys Ala Ile Gly Lys Leu Pro Ile Ala Met Arg Page 49

Ala val Thr Asn Tyr val Cys Leu Lys Glu Ala Tyr Glu Glu Gln Lys 260 270 Lys Lys Ala Ala Asp His Pro Asn Arg Thr Pro Ser Ile Trp Leu Ala 275 280 285 Met Tyr Arg Ala Phe Gly Arg Pro Ile Leu Leu Ser Ser Thr Phe Arg 290 295 300 Tyr Leu Ala Asp Leu Leu Gly Phe Ala Gly Pro Leu Cys Ile Ser Gly 305 315 320 ɪle val Gln Arg Val Asn Glu Pro Lys Asn Asn Thr Thr Arg Phe Ser 325 330 335 Glu Thr Leu Ser Ser Lys Glu Phe Leu Glu Asn Ala His Val Leu Ala 340 345 350 val Leu Leu Phe Leu Ala Leu Ile Leu Gln Arg Thr Phe Leu Gln Ala 355 365 Ser Tyr Tyr val Thr Ile Glu Thr Gly Ile Asn Leu Arg Gly Ala Leu 370 380 Leu Ala Met Ile Tyr Asn Lys Ile Leu Arg Leu Ser Thr Ser Asn Leu 385 390 400 Ser Met Gly Glu Met Thr Leu Gly Gln Ile Asn Asn Leu Val Ala Ile 405 410 415 Glu Thr Asn Gln Leu Met Trp Phe Leu Phe Leu Cys Pro Asn Leu Trp 420 430 Ala Met Pro Val Gln Ile Ile Met Gly Val Ile Leu Leu Tyr Asn Leu 435 445 Leu Gly Ser Ser Ala Leu val Gly Ala Ala val Ile val Leu Leu Ala 450 460 Pro Ile Gln Tyr Phe Ile Ala Thr Lys Leu Ala Glu Ala Gln Lys Ser 465 470 475 480 Thr Leu Asp Tyr Ser Thr Glu Arg Leu Lys Lys Thr Asn Glu Ile Leu 485 490 495

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660 665 670 Gly Tyr Phe Ser Trp Gly Ser Gly Leu Ala Thr Leu Ser Asn Ile Asp Ile Arg Ile Pro Thr Gly Gln Leu Thr Met Ile Val Gly Gln Val Gly 690 700 Cys Gly Lys Ser Ser Leu Leu Leu Ala Ile Leu Gly Glu Met Gln Thr 705 710 715 720 Leu Glu Gly Lys Val Tyr Trp Asn Asn Val Asn Glu Ser Glu Pro Ser Phe Glu Ala Thr Arg Ser Arg Ser Arg Tyr Ser Val Ala Tyr Ala Ala 740 745 750

### s263us104.st25

Gln Lys Pro Trp Leu Leu Asn Ala Thr Val Glu Glu Asn Ile Thr Phe 755 760 765 Gly Ser Ser Phe Asn Arg Gln Arg Tyr Lys Ala Val Thr Asp Ala Cys 770 780 Ser Leu Gln Pro Asp Ile Asp Leu Leu Pro Phe Gly Asp Gln Thr Glu 785 790 795 800 Ile Gly Glu Arg Gly Ile Asn Leu Ser Gly Gly Gln Arg Gln Arg Ile 805 810 815 Cys Val Ala Arg Ala Leu Tyr Gln Asn Thr Asn Ile Val Phe Leu Asp 820 825 830 Asp Pro Phe Ser Ala Leu Asp Ile His Leu Ser Asp His Leu Met Gln 845 Glu Gly Ile Leu Lys Phe Leu Gln Asp Asp Lys Arg Thr Val Val Leu 850 860 Val Thr His Lys Leu Gln Tyr Leu Thr His Ala Asp Trp Ile Ile Ala 865 870 875 Met Lys Asp Gly Ser Val Leu Arg Glu Gly Thr Leu Lys Asp Ile Gln 885 890 895 Thr Lys Asp Val Glu Leu Tyr Glu His Trp Lys Thr Leu Met Asn Arg  $900 \hspace{1.5cm} 905 \hspace{1.5cm} 910$ Gln Asp Gln Glu Leu Glu Lys Asp Met Glu Ala Asp Gln Thr Thr Leu 915 920 925 Glu Arg Lys Thr Leu Arg Arg Ala Met Tyr Ser Arg Glu Ala Lys Ala 930 935 940 Gln Met Glu Asp Glu Asp Glu Glu Glu Glu Glu Glu Asp Glu Asp 945 950 955 960 Asp Asn Met Ser Thr Val Met Arg Leu Arg Thr Lys Met Pro Trp Lys 965 970 975 Thr Cys Trp Trp Tyr Leu Thr Ser Gly Gly Phe Phe Leu Leu Phe Leu 980 985 990Met Ile Phe Ser Lys Leu Leu Lys His Ser Val Ile Val Ala Ile Asp 995 1000 1005 Page 52

### s263US104.ST25

Tyr Trp Leu Ala Thr Trp Thr Ser Glu Tyr Ser Ile Asn Asp Pro 1010 1020 Gly Lys Ala Asp Gln Thr Phe Tyr Val Ala Gly Phe Ser Ile Leu 1025 1030 1035 Cys Gly Ala Gly Ile Phe Leu Cys Leu Val Thr Ser Leu Thr Val Glu Trp Met Gly Leu Thr Ala Ala Lys Asn Leu His His Asn Leu 1055 1060 1065 Leu Asn Lys Ile Ile Leu Gly Pro Ile Arg Phe Phe Asp Thr Thr Pro Leu Gly Leu Ile Leu Asn Arg Phe Ser Ala Asp Thr Asn Ile 1085 1090 1095 Ile Asp Gln His Ile Pro Pro Thr Leu Glu Ser Leu Thr Arg Ser Thr Leu Leu Cys Leu Ser Ala Ile Gly Met Ile Ser Tyr Ala Thr Pro Val Phe Leu Ile Ala Leu Ala Pro Leu Gly Val Ala Phe Tyr 1130 1135 1140 Phe Ile Gln Lys Tyr Phe Arg Val Ala Ser Lys Asp Leu Gln Glu 1145 1150 1155 Leu Asp Asp Ser Thr Gln Leu Pro Leu Leu Cys His Phe Ser Glu 1160 1165 1170 Thr Ala Glu Gly Leu Thr Thr Ile Arg Ala Phe Arg His Glu Thr Arg Phe Lys Gln Arg Met Leu Glu Leu Thr Asp Thr Asn Asn Ile 1190 1195 1200 Ala Tyr Leu Phe Leu Ser Ala Ala Asn Arg Trp Leu Glu Val Arg 1205 1210 1215 Thr Asp Tyr Leu Gly Ala Cys Ile Val Leu Thr Ala Ser Ile Ala Ser Ile Ser Gly Ser Ser Asn Ser Gly Leu Val Gly Leu Gly Leu

Leu Tyr Ala Leu Thr Ile Thr Asn Tyr Leu Asn Trp Val Val Arg ASN Leu Ala ASP Leu Glu Val Gln Met Gly Ala Val Lys Lys Val Asn Ser Phe Leu Thr Met Glu Ser Glu Asn Tyr Glu Gly Thr Met Asp Pro Ser Gln Val Pro Glu His Trp Pro Gln Glu Gly Glu Ile 1295 1300 1305 Lys Ile His Asp Leu Cys Val Arg Tyr Glu Asn Asn Leu Lys Pro 1310 1315 1320 Val Leu Lys His Val Lys Ala Tyr Ile Lys Pro Gly Gln Lys Val Gly Ile Cys Gly Arg Thr Gly Ser Gly Lys Ser Ser Leu Ser Leu 1340 1345 Ala Phe Phe Arg Met Val Asp Ile Phe Asp Gly Lys Ile Val Ile 1355 1360 1365 Asp Gly Ile Asp Ile Ser Lys Leu Pro Leu His Thr Leu Arg Ser Arg Leu Ser Ile Ile Leu Gln Asp Pro Ile Leu Phe Ser Gly Ser Ile Arg Phe Asn Leu Asp Pro Glu Cys Lys Cys Thr Asp Asp Arg Leu Trp Glu Ala Leu Glu Ile Ala Gln Leu Lys Asn Met Val Lys 1415 1420 1425 Ser Leu Pro Gly Gly Leu Asp Ala Thr Val Thr Glu Gly Gly Glu 1430 1440 Asn Phe Ser Val Gly Gln Arg Gln Leu Phe Cys Leu Ala Arg Ala 1445 1450 1455 Phe Val Arg Lys Ser Ser Ile Leu Ile Met Asp Glu Ala Thr Ala 1460 1470

s263US104.ST25 Ser Ile Asp Met Ala Thr Glu Asn Ile Leu Gln Lys val Val Met 1475 1480 1485 Thr Ala Phe Ala Asp Arg Thr Val Val Thr Ile Ala His Arg Val Ser Ser Ile Met Asp Ala Gly Leu Val Leu Val Phe Ser Glu Gly Ile Leu Val Glu Cys Asp Thr Gly Pro Asn Leu Leu Gln His Lys 1520 1530 Asn Gly Leu Phe Ser Thr Leu Val Met Thr Asn Lys Gly Gly Gly 1535 1540 1545 Gly Gly Gly Met Leu Ser Arg Lys Gly Ile Ile Pro Glu Glu Tyr Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr Arg Thr Arg Glu Arg Arg Ala Arg Phe Val Ser Lys Lys Gly Asn Cys Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu Gln 1595 1600 1605 Asp Val Phe Thr Thr Leu Val Asp Leu Lys Trp Pro His Thr Leu 1610 1620 Leu Ile Phe Thr Met Ser Phe Leu Cys Ser Trp Leu Leu Phe Ala 1625 1630 1635 Met Val Trp Trp Leu Ile Ala Phe Ala His Gly Asp Leu Tyr Ala 1640 1650 1650 Tyr Met Glu Lys Gly Ile Thr Asp Leu Ala Pro Tyr Pro Tyr Asp 1655 1660 1665 Val Pro Asp Tyr Ala Gly Glu Gly Thr Asn Val Pro Cys Val Thr 1670 1680 Ser Ile His Ser Phe Ser Ser Ala Phe Leu Phe Ser Ile Glu Val 1685 1690 1695 Gln Val Thr Ile Gly Phe Gly Gly Arg Met Val Thr Glu Glu Cys 1700 1705 1710

### s263US104.ST25

Pro Leu Ala Ile Leu Ile Leu Ile Val Gln Asn Ile Val Gly Leu Met Ile Asn Ala Ile Met Leu Gly Cys Ile Phe Met Lys Thr Ala Gln Ala His Arg Arg Ala Glu Thr Leu Ile Phe Ser Lys His Ala Val Ile Thr Leu Arg His Gly Arg Leu Cys Phe Met Leu Arg Val Gly Asp Leu Arg Lys Ser Met Ile Ile Ser Ala Thr Ile His Met Gln Val Val Arg Lys Thr Thr Ser Pro Glu Gly Glu Val Val Pro 1790 1795 1800 Leu His Gln Val Asp Ile Pro Met Glu Asn Gly Val Gly Gly Asn 1805 1810 Gly Ile Phe Leu Val Ala Pro Leu Ile Ile Tyr His Val Ile Asp 1820 1825 1830 Ser Asn Ser Pro Leu Tyr Asp Leu Ala Pro Ser Asp Leu His His His Gln Asp Leu Glu Ile Ile Val Ile Leu Glu Gly Val Val Glu Thr Thr Gly Ile Thr Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp 1865 1870 1875 Glu Ile Leu Trp Gly Gln Arg Phe Val Pro Ile Val Ala Glu Glu 1880 1885 1890 Asp Gly Arg Tyr Ser Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile 1895 1900 1905 Lys Val Pro Thr Pro Leu Cys Thr Ala Arg Gln Leu Asp Glu Asp 1910 1920 Arg Ser Leu Leu Asp Ala Leu Thr Leu Ala Ser Ser Arg Gly Pro 1925 1930 1935 Leu Arg Lys Arg Ser Val Ala Val Ala Lys Ala Lys Pro Lys Phe 1940 1945 1950 Page 56

Ser Ile Ser Pro Asp Ser Leu Ser 1955 1960

<210> 8 <211> 1947 <212> PRT

<213> Homo sapiens

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# s263us104.st25

Pro Glu Ser Ser Ala Ser Phe Leu Ser Arg Ile Thr Phe Trp Trp Ile 210 220Thr Gly Leu Ile Val Arg Gly Tyr Arg Gln Pro Leu Glu Gly Ser Asp 225 230 235 240 Leu Trp Ser Leu Asn Lys Glu Asp Thr Ser Glu Gln Val Val Pro Val 245 250 250 Leu Val Lys Asn Trp Lys Lys Glu Cys Ala Lys Thr Arg Lys Gln Pro 260 265 270 Val Lys Val Val Tyr Ser Ser Lys Asp Pro Ala Gln Pro Lys Glu Ser 275 280 285 Ser Lys Val Asp Ala Asn Glu Glu Val Glu Ala Leu Ile Val Lys Ser 290 295 300 Pro Gln Lys Glu Trp Asn Pro Ser Leu Phe Lys Val Leu Tyr Lys Thr 305 310 315 320Phe Gly Pro Tyr Phe Leu Met Ser Phe Phe Phe Lys Ala Ile His Asp 325 330 335 Leu Met Met Phe Ser Gly Pro Gln Ile Leu Lys Leu Leu Ile Lys Phe 340 345 Val Asn Asp Thr Lys Ala Pro Asp Trp Gln Gly Tyr Phe Tyr Thr Val 355 Leu Leu Phe Val Thr Ala Cys Leu Gln Thr Leu Val Leu His Gln Tyr 370 375 Phe His Ile Cys Phe Val Ser Gly Met Arg Ile Lys Thr Ala Val Ile 385 390 400 Gly Ala Val Tyr Arg Lys Ala Leu Val Ile Thr Asn Ser Ala Arg Lys 405 410 415Ser Ser Thr Val Gly Glu Ile Val Asn Leu Met Ser Val Asp Ala Gln 420 425 Arg Phe Met Asp Leu Ala Thr Tyr Ile Asn Met Ile Trp Ser Ala Pro 435Leu Gln Val Ile Leu Ala Leu Tyr Leu Leu Trp Leu Asn Leu Gly Pro Page 58

Ser Val Leu Ala Gly Val Ala Val Met Val Leu Met Val Pro Val Asn 465 470 475 480 Ala val Met Ala Met Lys Thr Lys Thr Tyr Gln Val Ala His Met Lys 485 490 495 Ser Lys Asp Asn Arg Ile Lys Leu Met Asn Glu Ile Leu Asn Gly Ile Lys Val Leu Lys Leu Tyr Ala Trp Glu Leu Ala Phe Lys Asp Lys Val Leu Ala Ile Arg Gln Glu Glu Leu Lys Val Leu Lys Lys Ser Ala Tyr 530 540 Leu Ser Ala Val Gly Thr Phe Thr Trp Val Cys Thr Pro Phe Leu Val 545 550 560 Ala Leu Cys Thr Phe Ala Val Tyr Val Thr Ile Asp Glu Asn Asn Ile 565 570 575 Leu Asp Ala Gln Thr Ala Phe Val Ser Leu Ala Leu Phe Asn Ile Leu 580 585 590 Arg Phe Pro Leu Asn Ile Leu Pro Met Val Ile Ser Ser Ile Val Gln 595 600 605 Ala Ser Val Ser Leu Lys Arg Leu Arg Ile Phe Leu Ser His Glu Glu Leu Glu Pro Asp Ser Ile Glu Arg Arg Pro Val Lys Asp Gly Gly Gly 625 630 635 Thr Asn Ser Ile Thr Val Arg Asn Ala Thr Phe Thr Trp Ala Arg Ser
645 650 655 Asp Pro Pro Thr Leu Asn Gly Ile Thr Phe Ser Ile Pro Glu Gly Ala 660 665 670 Leu Val Ala Val Val Gly Gln Val Gly Cys Gly Lys Ser Ser Leu Leu 675 680 685 Ser Ala Leu Leu Ala Glu Met Asp Lys Val Glu Gly His Val Ala Ile 690 700

# Lys Gly Ser Val Ala Tyr Val Pro Gln Gln Ala Trp Ile Gln Asn Asp 705 Ser Leu Arg Glu Asn Ile Leu Phe Gly Cys Gln Leu Glu Glu Pro Tyr 725 Tyr Arg Ser Val Ile Gln Ala Cys Ala Leu Leu Pro Asp Leu Glu Ile 745

Leu Pro Ser Gly Asp Arg Thr Glu Ile Gly Glu Lys Gly Val Asn Leu 765

Ser Gly Gly Gln Lys Gln Arg Val Ser Leu Ala Arg Ala Val Tyr Ser 770

Asn Ala Asp Ile Tyr Leu Phe Asp Asp Pro Leu Ser Ala Val Asp Ala 785 795 800

His Val Gly Lys His Ile Phe Glu Asn Val Ile Gly Pro Lys Gly Met 815 Leu Lys Asn Lys Thr Arg Ile Leu Val Thr His Ser Met Ser Tyr Leu 825 820 820

Pro Gln val Asp Val Ile Ile Val Met Ser Gly Gly Lys Ile Ser Glu 835 840 845

Met GJy Ser Tyr GJn Glu Leu Leu Ala Arg ASp GJy Ala Phe Ala GJu 850 860

Phe Leu arg Thr Tyr Ala Ser Thr Glu Gln Glu Gln Asp Ala Glu Glu 865 870 875 Asn Gly Val Thr Kasa Ser Gly Pro Gly Lys Glu Ala Lys Gln Met 885 890 895

Glu Asn Gly Met Leu Val Thr Asp Ser Ala Gly Lys Gln Leu Gln Arg 900 905

Gln Leu Ser Ser Ser Ser Ser Tyr Ser Gly Asp Ile Ser Arg His His 915 925

Asn Ser Thr Ala Glu Leu Gln Lys Ala Glu Ala Lys Lys Glu Glu Thr 930

Trp Lys Leu Met Glu Ala Asp Lys Ala Gln Thr Gly Gln Val Lys Leu 945

950

960

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Ser Val Tyr Trp Asp Tyr Met Lys Ala Ile Gly Leu Phe Ile Ser Phe 965 970 975 Leu Ser Ile Phe Leu Phe Met Cys Asn His Val Ser Ala Leu Ala Ser Asn Tyr Trp Leu Ser Leu Trp Thr Asp Asp Pro Ile Val Asn Gly Thr  $995 \ \ \, 1000 \ \ \, 1005$ Gln Glu His Thr Lys Val Arg Leu Ser Val Tyr Gly Ala Leu Gly 1010 1015 1020 Ile Ser Gln Gly Ile Ala Val Phe Gly Tyr Ser Met Ala Val Ser Ile Gly Gly Ile Leu Ala Ser Arg Cys Leu His Val Asp Leu Leu His Ser Ile Leu Arg Ser Pro Met Ser Phe Phe Glu Arg Thr Pro 1055 1060 1065 Ser Gly Asn Leu Val Asn Arg Phe Ser Lys Glu Leu Asp Thr Val Asp Ser Met Ile Pro Glu Val Ile Lys Met Phe Met Gly Ser Leu Phe Asn Val Ile Gly Ala Cys Ile Val Ile Leu Leu Ala Thr Pro 1100 1105 1110 Ile Ala Ala Ile Ile Ile Pro Pro Leu Gly Leu Ile Tyr Phe Phe 1115 1120 1125 Val Gln Arg Phe Tyr Val Ala Ser Ser Arg Gln Leu Lys Arg Leu 1130 1140 Glu Ser Val Ser Arg Ser Pro Val Tyr Ser His Phe Asn Glu Thr 1145 1150 1155 Leu Leu Gly Val Ser Val Ile Arg Ala Phe Glu Glu Gln Glu Arg Phe Ile His Gln Ser Asp Leu Lys Val Asp Glu Asn Gln Lys Ala 1175 1180 1185 Tyr Tyr Pro Ser Ile Val Ala Asn Arg Trp Leu Ala Val Arg Leu 1190 1195 1200

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Glu Cys Val Gly Asn Cys Ile Val Leu Phe Ala Ala Leu Phe Ala 1205 1210 1215 Val Ile Ser Arg His Ser Leu Ser Ala Gly Leu Val Gly Leu Ser 1220 1230 Val Ser Tyr Ser Leu Gln Val Thr Thr Tyr Leu Asn Trp Leu Val 1235 1240 1245 Arg Met Ser Ser Glu Met Glu Thr Asn Ile Val Ala Val Glu Arg 1250 1260 Leu Lys Glu Tyr Ser Glu Thr Glu Lys Glu Ala Pro Trp Gln Ile 1265 Trp Gln Ile Gln Glu Thr Ala Pro Pro Ser Ser Trp Pro Gln Val Gly Arg Val 1280 1285 1290 Glu Phe Arg Asn Tyr Cys Leu Arg Tyr Arg Glu Asp Leu Asp Phe 1305 Val Leu Arg His Ile Asn Val Thr Ile Asn Gly Gly Glu Lys Val 1310 1320 Gly Ile Val Gly Arg Thr Gly Ala Gly Lys Ser Ser Leu Thr Leu 1325 1330 1335 Gly Leu Phe Arg Ile Asn Glu Ser Ala Glu Gly Glu Ile Ile Ile 1340 1350 Asp Gly Ile Asn Ile Ala Lys Ile Gly Leu His Asp Leu Arg Phe 1355 Lys Ile Thr Ile Ile Pro Gln Asp Pro Val Leu Phe Ser Gly Ser 1370 1380 Leu Arg Met Asn Leu Asp Pro Phe Ser Gln Tyr Ser Asp Glu Glu 1385 1390 1395 Val Trp Thr Ser Leu Glu Leu Ala His Leu Lys Asp Phe Val Ser 1400 1405 1410 Ala Leu Pro Asp Lys Leu Asp His Glu Cys Ala Glu Gly Gly Glu 1415 1420 1425 Asn Leu Ser Val Gly Gln Arg Gln Leu Val Cys Leu Ala Arg Ala

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Leu Leu Arg Lys Thr Lys Ile Leu Val Leu Asp Glu Ala Thr Ala Ala Val Asp Leu Glu Thr Asp Asp Leu Ile Gln Ser Thr Ile Arg 1460 1465 1470 Thr Gln Phe Glu Asp Cys Thr Val Leu Thr Ile Ala His Arg Leu Asn Thr Ile Met Asp Tyr Thr Arg Val Ile Val Leu Asp Lys Gly 1490 1495 1500 Glu Ile Gln Glu Tyr Gly Ala Pro Ser Asp Leu Leu Gln Gln Arg 1505 1510 1515 Gly Leu Phe Tyr Ser Met Ala Lys Asp Ala Gly Leu Val Gly Gly 1520 1530 Gly Gly Gly Met Leu Ser Arg Lys Gly Ile Ile Pro Glu Glu 1535 1540 1545 Tyr Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr Arg Thr Arg Glu Arg Arg Ala Arg Phe Val Ser Lys Lys Gly Asn 1565 1570 1575 Cys Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu 1580 1590 Gln Asp Val Phe Thr Thr Leu Val Asp Leu Lys Trp Pro His Thr 1595 1600 1605 Leu Leu Ile Phe Thr Met Ser Phe Leu Cys Ser Trp Leu Leu Phe 1610 1620Ala Met Val Trp Trp Leu Ile Ala Phe Ala His Gly Asp Leu Tyr 1625 1630 1635 Ala Tyr Met Glu Lys Gly Ile Thr Asp Leu Ala Pro Tyr Pro Tyr
1640 1650 Asp Val Pro Asp Tyr Ala Gly Glu Gly Thr Asn Val Pro Cys Val

Thr	Ser 1670	ıle	ніѕ	Ser	Phe	Ser 1675	ser	s26 Ala	3US1 Phe	.04 . s Leu	T25 Phe 1680	Ser	Ile	Glu
۷a٦	Gln 1685	val	Thr	Ile	Gly	Phe 1690	G] y	GТу	Arg	Met	val 1695	Thr	Glu	Glu
Cys	Pro 1700	Leu	Αla	Ile	Leu	Ile 1705	Leu	Ile	val	Gln	Asn 1710	Ile	۷al	Gly
Leu	Met 17 <b>1</b> 5	Ile	Asn	۸la	Ile	Met 1720	Leu	GТу	Cys	Ile	Phe 1725	Met	Lys	Thr
Аlа	G]n 1730	Αla	ніѕ	Arg	Arg	Ala 1735	Glu	Thr	Leu	Ile	Phe 1740	Ser	Lys	ніѕ
Ala	Val 1745	Ile	Thr	Leu	Arg	ніs 1750	GЗу	Arg	Leu	Cys	Phe 1755	Met	Leu	Arg
val	Gly 1760	Asp	Leu	Arg	Lys	Ser 1765	Met	Ile	Ile	ser	Ala 1770	Thr	Ile	His
Met	Gln 1775	Val	Val	Arg	Lys	Thr 1780	Thr	ser	Pro	Glu	Gly 1785	G1u	val	۷al
Pro	Leu 1790	His	G∏n	val	Asp	Ile 1795	Pro	Met	Glu	Asn	Gly 1800	val	Gly	Gly
Asn	Gly 1805	Ile	Phe	Leu	Val	Ala 1810	Pro	Leu	Ile	Ile	туг 1815	His	val	Ile
Asp	Ser 1820	Asn	Ser	Pro	Leu	Tyr 1825	Asp	Leu	Ala	Pro	ser 1830	Asp	Leu	нis
ніѕ	ніs 1835	Gln	Asp	Leu	Glu	Ile 1840	Ile	Val	Ile	Leu	Glu 1845	Gly	Val	۷al
Glu	Thr 1850	Thr	GТу	Ile	Thr	Thr 1855	G∏n	Ala	Arg	Thr	Ser 1860	туг	Leu	Αla
Asp	G]u 1865	Ile	Leu	Trp	Gly	Gln 1870	Arg	Phe	۷al	Pro	Ile 1875	val	Αla	Glu
G1 u	Asp 1880	Gly	Arg	Tyr	Ser	Val 1885	Asp	Tyr	Ser	Lys	Phe 1890	Gly	Asn	Thr
Ile	Lys 1895	۷al	Pro	Thr	Pro	Leu 1900	Cys	Thr	Ala	Arg	Gln 1905	Leu	Asp	Glu

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Asp Arg Ser Leu Leu Asp Ala Leu Thr Leu Ala Ser Ser Arg Gly 1910  $^{\circ}$ 

Pro Leu Arg Lys Arg Ser Val Ala Val Ala Lys Ala Lys Pro Lys 1925 1930 1935

Phe Ser Ile Ser Pro Asp Ser Leu Ser 1940 1945

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<212> PRT

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ile Asp Gly Val ile Leu Asn Leu Ser Ala ile Phe Met ile Thr Phe 35 40 45

Gly Ile Arg Asp Leu Val Asn Leu Cys Lys Lys Lys His Ser Gly Ile 50 60

Lys Tyr Arg Arg Asn Trp Ile Ile Val Ser Arg Met Ala Leu Val Leu 65 70 75 80

Leu Glu Ile Ala Phe Val Ser Leu Ala Ser Leu Asn Ile Ser Lys Glu 85 90 95

Glu Ala Glu Asn Phe Thr Ile Val Ser Gln Tyr Ala Ser Thr Met Leu 100 110

Ser Leu Phe Val Ala Leu Ala Leu His Trp Ile Glu Tyr Asp Arg Ser 115 120 125

Val Val Ala Asn Thr Val Leu Leu Phe Tyr Trp Leu Phe Glu Thr Phe 130 140

Gly Asn Phe Ala Lys Leu Ile Asn Ile Leu Ile Arg His Thr Tyr Glu 145  $\cdot$  150  $\cdot$  160

Gly Ile Trp Tyr Ser Gly Gln Thr Gly Phe Ile Leu Thr Leu Phe Gln 175

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Val Ile Thr Cys Ala Ser Ile Leu Leu Leu Glu Ala Leu Pro Lys Lys 180 185 190 Pro Leu Met Pro His Gln His Ile His Gln Thr Leu Thr Arg Arg Lys 195 200 205 Pro Asn Pro Tyr Asp Ser Ala Asn Ile Phe Ser Arg Ile Thr Phe Ser Trp Met Ser Gly Leu Met Lys Thr Gly Tyr Glu Lys Tyr Leu Val Glu 225 230 235 240 Ala Asp Leu Tyr Lys Leu Pro Arg Asn Phe Ser Ser Glu Glu Leu Ser Gln Lys Leu Glu Lys Asn Trp Glu Asn Glu Leu Lys Gln Lys Ser Asn 260 265 270 Pro Ser Leu Ser Trp Ala Ile Cys Arg Thr Phe Gly Ser Lys Met Leu Leu Ala Ala Phe Phe Lys Ala Ile His Asp Val Leu Ala Phe Thr Gln Pro Gln Leu Leu Arg Ile Leu Ile Lys Phe Val Thr Asp Tyr Asn Ser 310 315 320Glu Arg Gln Asp Asp His Ser Ser Leu Gln Gly Phe Glu Asn Asn His Pro Gln Lys Leu Pro Ile Val Arg Gly Phe Leu Ile Ala Phe Ala Met 340 345 350 Phe Leu Val Gly Phe Thr Gln Thr Ser Val Leu His Gln Tyr Phe Leu 355 360 365Asn Val Phe Asn Thr Gly Met Tyr Ile Lys Ser Ala Leu Thr Ala Leu 370 380 Ile Tyr Gln Lys Ser Leu Val Leu Ser Asn Glu Ala Ser Gly Leu Ser Ser Thr Gly Asp Ile Val Asn Leu Met Ser Val Asp Val Gln Lys Leu
410 415 Gln Asp Leu Thr Gln Trp Leu Asn Leu Ile Trp Ser Gly Pro Phe Gln
420 425 430

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Ile Ile Cys Leu Tyr Ser Leu Tyr Lys Leu Leu Gly Asn Ser Met Trp Val Gly Val Ile Ile Leu Val Ile Met Met Pro Leu Asn Ser Phe 450 455 460 Leu Met Arg Ile Gln Lys Lys Leu Gln Lys Ser Gln Met Lys Tyr Lys 465 470 475 480 Asp Glu Arg Thr Arg Val Ile Ser Glu Ile Leu Asn Asn Ile Lys Ser Leu Lys Leu Tyr Ala Trp Glu Lys Pro Tyr Arg Glu Lys Leu Glu Glu 500 505 510 Val Arg Asn Asn Lys Glu Leu Lys Asn Leu Thr Lys Leu Gly Cys Tyr Met Ala Val Thr Ser Phe Gln Phe Asn Ile Val Pro Phe Leu Val Ser Cys Cys Thr Phe Ala Val Phe Val Tyr Thr Glu Asp Arg Ala Leu Thr Thr Asp Leu Val Phe Pro Ala Leu Thr Leu Phe Asn Leu Leu Ser Phe 565 570 575 Pro Leu Met Ile Ile Pro Met Val Leu Asn Ser Phe Ile Glu Ala Ser Val Ser Ile Gly Arg Leu Phe Thr Phe Phe Thr Asn Glu Glu Leu Gln
595 600 605 Pro Asp Ser Val Gln Arg Leu Pro Lys Val Lys Asn Ile Gly Asp Val Ala Ile Asn Ile Gly Asp Asp Ala Thr Phe Leu Trp Gln Arg Lys Pro Glu Tyr Lys Val Ala Leu Lys Asn Ile Asn Phe Gln Ala Lys Lys Gly
645 650 655 Asn Leu Thr Cys Ile Val Gly Lys Val Gly Ser Gly Lys Thr Ala Leu 660 670 Leu Ser Cys Met Leu Gly Asp Arg Phe Arg Val Lys Gly Phe Ala Thr Page 67

Val His Gly Ser Val Ala Tyr Val Ser Gln Val Pro Trp Ile Met Asn 690 695 700 Gly Thr Val Lys Glu Asn Ile Leu Phe Gly His Arg Tyr Asp Ala Glu 705 710 720 720 Phe Tyr Glu Lys Thr Ile Lys Ala Cys Ala Leu Thr Ile Asp Leu Ala Ile Leu Met Asp Gly Asp Lys Thr Leu Val Gly Glu Lys Gly Ile Ser 740 745 750 Leu Ser Gly Gly Gln Lys Ala Arg Leu Ser Leu Ala Arg Ala Val Tyr Ala Arg Ala Asp Thr Tyr Leu Leu Asp Asp Pro Leu Ala Ala Val Asp Glu His Val Ala Arg His Leu Ile Glu His Val Leu Gly Pro Asn Gly 785 790 795 800 Leu Leu His Thr Lys Thr Lys Val Leu Ala Thr Asn Lys Val Ser Ala Leu Ser Ile Ala Asp Ser Ile Ala Leu Leu Asp Asn Gly Glu Ile Thr 820 825 830 Gln Gln Gly Thr Tyr Asp Glu Ile Thr Lys Asp Ala Asp Ser Pro Leu 835 840 845 Trp Lys Leu Leu Asn Asn Tyr Gly Lys Lys Asn Asn Gly Lys Ser Asn Glu Phe Gly Asp Ser Ser Glu Ser Ser Val Arg Glu Ser Ser Ile Pro 865 870 875 880 Val Glu Gly Glu Leu Glu Gln Leu Gln Lys Leu Asn Asp Leu Asp Phe 885 890 895 Gly Asn Ser Asp Ala Ile Ser Leu Arg Arg Ala Ser Asp Ala Thr Leu Gly Ser Ile Asp Phe Gly Asp Asp Glu Asn Ile Ala Lys Arg Glu His

s263Us104.ST25 Arg Glu Gln Gly Lys Val Lys Trp Asn Ile Tyr Leu Glu Tyr Ala Lys 930 935 940 Ala Cys Asn Pro Lys Ser Val Cys Val Phe Ile Leu Phe Ile Val Ile Ser Met Phe Leu Ser Val Met Gly Asn Val Trp Leu Lys His Trp Ser Glu Val Asn Ser Arg Tyr Gly Ser Asn Pro Asn Ala Ala Arg Tyr Leu Ala Ile Tyr Phe Ala Leu Gly Ile Gly Ser Ala Leu Ala Thr Leu Ile 995 1000 1005 Gln Thr Ile Val Leu Trp Val Phe Cys Thr Ile His Ala Ser Lys Tyr Leu His Asn Leu Met Thr Asn Ser Val Leu Arg Ala Pro Met 1025 1030 1035 Thr Phe Phe Glu Thr Thr Pro Ile Gly Arg Ile Leu Asn Arg Phe 1040 1045 1050 Ser Asn Asp Ile Tyr Lys Val Asp Ala Leu Leu Gly Arg Thr Phe 1055 1065 Ser Gln Phe Phe Val Asn Ala Val Lys Val Thr Phe Thr Ile Thr Val Ile Cys Ala Thr Thr Trp Gln Phe Ile Phe Ile Ile Ile Pro Leu Ser Val Phe Tyr Ile Tyr Tyr Gln Gln Tyr Tyr Leu Arg Thr Ser Arg Glu Leu Arg Arg Leu Asp Ser Ile Thr Arg Ser Pro Ile Tyr Ser His Phe Gln Glu Thr Leu Gly Gly Leu Ala Thr Val Arg 1130 1135 1140 Gly Tyr Ser Gln Gln Lys Arg Phe Ser His Ile Asn Gln Cys Arg 

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Arg Trp Leu Ala Tyr Arg Leu Glu Leu Ile Gly Ser Ile Ile Ile Leu Gly Ala Ala Thr Leu Ser Val Phe Arg Leu Lys Gln Gly Thr Leu Thr Ala Gly Met Val Gly Leu Ser Leu Ser Tyr Ala Leu Gln Ile Thr Gln Thr Leu Asn Trp Ile Val Arg Met Thr Val Glu Val 1220 1230 Glu Thr Asn Ile Val Ser Val Glu Arg Ile Lys Glu Tyr Ala Asp 1235 1240 1245 Leu Lys Ser Glu Ala Pro Leu Ile Val Glu Gly His Arg Pro Pro Lys Glu Trp Pro Ser Gln Gly Asp Ile Lys Phe Asn Asn Tyr Ser Thr Arg Tyr Arg Pro Glu Leu Asp Leu Val Leu Lys His Ile Asn 1280 1290 Ile His Ile Lys Pro Asn Glu Lys Val Gly Ile Val Gly Arg Thr 1295 1300 1305 Gly Ala Gly Lys Ser Ser Leu Thr Leu Ala Leu Phe Arg Met Ile Glu Ala Ser Glu Gly Asn Ile Val Ile Asp Asn Ile Ala Ile Asn 1375 1330 1335 Glu Ile Gly Leu Tyr Asp Leu Arg His Lys Leu Ser Ile Ile Pro Gln Asp Ser Gln Val Phe Glu Gly Thr Val Arg Glu Asn Ile Asp 1355 1360 1365 Pro Ile Asn Gln Tyr Thr Asp Glu Ala Ile Trp Arg Ala Leu Glu Leu Ser His Leu Lys Glu His Val Leu Ser Met Ser Asn Asp Gly 1385 1390 1395 Leu Asp. Ala Gln Leu Thr Glu Gly Gly Gly Asn Leu Ser Val Gly  $1400 \\ 1400 \\ Page 70$ 

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Gln Arg Gln Leu Leu Cys Leu Ala Arg Ala Met Leu Val Pro Ser 1415 1420 1425 Lys Ile Leu Val Leu Asp Glu Ala Thr Ala Ala Val Asp Val Glu Thr Asp Lys Val Val Gln Glu Thr Ile Arg Thr Ala Phe Lys Asp 1445 1450 1455 Arg Thr Ile Leu Thr Ile Ala His Arg Leu Asn Thr Ile Met Asp 1460 1465 1470 Ser Asp Arg Ile Ile Val Leu Asp Asn Gly Lys Val Ala Glu Phe Asp Ser Pro Gly Gln Leu Leu Ser Asp Asn Lys Ser Leu Phe Tyr Ser Leu Cys Met Glu Ala Gly Leu Val Asn Glu Asn Gly Gly Gly 1505 1510 1515 Gly Gly Met Leu Ser Arg Lys Gly Ile Ile Pro Glu Glu Tyr Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr Arg 1535 1540 1545 Thr Arg Glu Arg Arg Ala Arg Phe Val Ser Lys Lys Gly Asn Cys 1550 1560 Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu Gln Asp Val Phe Thr Thr Leu Val Asp Leu Lys Trp Pro His Thr Leu 1580 1590 Leu Ile  $\,$  Phe Thr Met Ser Phe  $\,$  Leu Cys Ser Trp Leu Leu Phe Ala  $\,$  1595  $\,$   $\,$  1600  $\,$ Met Val Trp Trp Leu Ile Ala Phe Ala His Gly Asp Leu Tyr Ala 1610 1615 1620 Tyr Met Glu Lys Gly Ile Thr Asp Leu Ala Pro Tyr Pro Tyr Asp 1625 1630 1635 Val Pro Asp Tyr Ala Gly Glu Gly Thr Asn Val Pro Cys Val Thr Ser Ile His Ser Phe Ser Ser Ala Phe Leu Phe Ser Ile Glu Val Gln Val Thr Ile Gly Phe Gly Gly Arg Met Val Thr Glu Glu Cys Pro Leu Ala Ile Leu Ile Leu Ile Val Gln Asn Ile Val Gly Leu 1685 1690 1695 Met Ile Asn Ala Ile Met Leu Gly Cys Ile Phe Met Lys Thr Ala Gln Ala His Arg Arg Ala Glu Thr Leu Ile Phe Ser Lys His Ala Val Ile Thr Leu Arg His Gly Arg Leu Cys Phe Met Leu Arg Val Gly Asp Leu Arg Lys Ser Met  $\mbox{ lle Ile Ser Ala Thr}$   $\mbox{ lle His Met}$   $\mbox{ 1745}$ Gln Val Val Arg Lys Thr Thr Ser Pro Glu Gly Glu Val Val Pro 1760 1765 1770 Leu His Gln Val Asp Ile Pro Met Glu Asn Gly Val Gly Gly Asn Gly Ile Phe Leu Val Ala Pro Leu Ile Ile Tyr His Val Ile Asp 1790 1795 1800 Ser Asn Ser Pro Leu Tyr Asp Leu Ala Pro Ser Asp Leu His His His Gln Asp Leu Glu Ile Ile Val Ile Leu Glu Gly Val Val Glu 1820 1825 1830 Thr Thr Gly Ile Thr Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp 1835 1840 1845 Glu Ile Leu Trp Gly Gln Arg Phe Val Pro Ile Val Ala Glu Glu
1850 1860 Asp Gly Arg Tyr Ser Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile 1865 1870 1875

1645

S263US104.ST25
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Val Ile Thr Cys Ala Ser Ile Leu Leu Leu Glu Ala Leu Pro Lys Lys 180 185 190

s263uS104.ST25 Pro Leu Met Pro His Gln His Ile His Gln Thr Leu Thr Arg Arg Lys 195 200 205 Pro Asn Pro Tyr Asp Ser Ala Asn Ile Phe Ser Arg Ile Thr Phe Ser 210 215 220 Trp Met Ser Gly Leu Met Lys Thr Gly Tyr Glu Lys Tyr Leu val Glu 225 230 235 240 Ala Asp Leu Tyr Lys Leu Pro Arg Asn Phe Ser Ser Glu Glu Leu Ser 245 250 250 Gln Lys Leu Glu Lys Asn Trp Glu Asn Glu Leu Lys Gln Lys Ser Asn 260 265 270 Pro Ser Leu Ser Trp Ala Ile Cys Arg Thr Phe Gly Ser Lys Met Leu 275 280 285 Leu Ala Ala Phe Phe Lys Ala Ile His Asp Val Leu Ala Phe Thr Gln 290 300 Pro Gln Leu Leu Arg Ile Leu Ile Lys Phe val Thr Asp Tyr Asn Ser 305  $\phantom{\bigg|}310\phantom{\bigg|}$  315 Thr Asp Tyr Asn Ser 320 Glu Arg Gln Asp Asp His Ser Ser Leu Gln Gly Phe Glu Asn Asn His 325 330 335 Pro Gln Lys Leu Pro Ile Val Arg Gly Phe Leu Ile Ala Phe Ala Met 340 350 Phe Leu Val Gly Phe Thr Gln Thr Ser Val Leu His Gln Tyr Phe Leu 355 360 365 Asn val Phe Asn Thr Gly Met Tyr Ile Lys Ser Ala Leu Thr Ala Leu 370 380 Ile Tyr Gln Lys Ser Leu Val Leu Ser Asn Glu Ala Ser Gly Leu Ser 385 395 400 Ser Thr Gly Asp Ile val Asn Leu Met Ser val Asp val Gln Lys Leu 415 415 Gln Asp Leu Thr Gln Trp Leu Asn Leu Ile Trp Ser Gly Pro Phe Gln
420 425 430 Ile Ile Ile Cys Leu Tyr Ser Leu Tyr Lys Leu Leu Gly Asn Ser Met 445 445

Trp Val Gly Val Ile Ile Leu Val Ile Met Met Pro Leu Asn Ser Phe 450 460 Leu Met Arg Ile Gln Lys Lys Leu Gln Lys Ser Gln Met Lys Tyr Lys 465 470 475 480 Asp Glu Arg Thr Arg Val Ile Ser Glu Ile Leu Asn Asn Ile Lys Ser 495 490 Leu Lys Leu Tyr Ala Trp Glu Lys Pro Tyr Arg Glu Lys Leu Glu Glu 500 501 Val Arg Asn Asn Lys Glu Leu Lys Asn Leu Thr Lys Leu Gly Cys Tyr 515 525 525 Met Ala Val Thr Ser Phe Gln Phe Asn Ile Val Pro Phe Leu Val Ser 530 540 Cys Cys Thr Phe Ala Val Phe Val Tyr Thr Glu Asp Arg Ala Leu Thr 545 550 560 Thr Asp Leu Val Phe Pro Ala Leu Thr Leu Phe Asn Leu Leu Ser Phe 575 575 Pro Leu Met Ile Ile Pro Met Val Leu Asn Ser Phe Ile Glu Ala Ser 580 590 Val Ser Ile Gly Arg Leu Phe Thr Phe Phe Thr Asn Glu Glu Leu Gln 595 600 605 Pro Asp Ser Val Gln Arg Leu Pro Lys Val Lys Asn Ile Gly Asp Val Ala Ile Asn Ile Gly Asp Asp Ala Thr Phe Leu Trp Gln Arg Lys Pro 625 630 635 640 Glu Tyr Lys Val Ala Leu Lys Asn Ile Asn Phe Gln Ala Lys Lys Gly 645 650 655 Asn Leu Thr Cys Ile Val Gly Lys Val Gly Ser Gly Lys Thr Ala Leu 660 665 670 Leu Ser Cys Met Leu Gly Asp Arg Phe Arg Val Lys Gly Phe Ala Thr 675 685 Val His Gly Ser Val Ala Tyr Val Ser Gln Val Pro Trp Ile Met Asn 690 700 Page 75

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Gly Thr Val Lys Glu Asn Ile Leu Phe Gly His Arg Tyr Asp Ala Glu Phe Tyr Glu Lys Thr Ile Lys Ala Cys Ala Leu Thr Ile Asp Leu Ala Ile Leu Met Asp Gly Asp Lys Thr Leu Val Gly Glu Lys Gly Ile Ser Leu Ser Gly Gly Gln Lys Ala Arg Leu Ser Leu Ala Arg Ala Val Tyr Ala Arg Ala Asp Thr Tyr Leu Leu Asp Asp Pro Leu Ala Ala Val Asp Glu His Val Ala Arg His Leu Ile Glu His Val Leu Gly Pro Asn Gly Leu Leu His Thr Lys Thr Lys Val Leu Ala Thr Asn Lys Val Ser Ala 805 810 815 Leu Ser Ile Ala Asp Ser Ile Ala Leu Leu Asp Asn Gly Glu Ile Thr Gln Gln Gly Thr Tyr Asp Glu Ile Thr Lys Asp Ala Asp Ser Pro Leu 835 840 845 Trp Lys Leu Leu Asn Asn Tyr Gly Lys Lys Asn Asn Gly Lys Ser Asn Glu Phe Gly Asp Ser Ser Glu Ser Ser Val Arg Glu Ser Ser Ile Pro Val Glu Gly Glu Leu Glu Gln Leu Gln Lys Leu Asn Asp Leu Asp Phe Gly Asn Ser Asp Ala Ile Ser Leu Arg Arg Ala Ser Asp Ala Thr Leu Gly Ser Ile Asp Phe Gly Asp Asp Glu Asn Ile Ala Lys Arg Glu His Arg Glu Gln Gly Lys Val Lys Trp Asn Ile Tyr Leu Glu Tyr Ala Lys 930 940 Ala Cys Asn Pro Lys Ser Val Cys Val Phe Ile Leu Phe Ile Val Ile Page 76

950

Ser Met Phe Leu Ser Val Met Gly Asn Val Trp Leu Lys His Trp Ser 970 975 Glu Val Asn Ser Arg Tyr Gly Ser Asn Pro Asn Ala Ala Arg Tyr Leu 980 985 Ala Ile Tyr Phe Ala Leu Gly Ile Gly Ser Ala Leu Ala Thr Leu Ile 995 1000 1005 Gln Thr Ile Val Leu Trp Val Phe Cys Thr Ile His Ala Ser Lys 1010 1020 Tyr Leu His Asn Leu Met Thr Asn Ser Val Leu Arg Ala Pro Met 1025 1030 1035 Thr Phe Phe Glu Thr Thr Pro 1le Gly Arg Ile Leu Asn Arg Phe 1040 1045Ser Asn Asp Ile Tyr Lys Val Asp Ala Leu Leu Gly Arg Thr Phe 1055 1060 1065 Ser Gln Phe Phe Val Asn Ala Val Lys Val Thr Phe Thr Ile Thr 1070 1080 Val Ile Cys Ala Thr Thr Trp Gln Phe Ile Phe Ile Ile Ile Pro 1085 1090 1095 Leu Ser Val Phe Tyr Ile Tyr Tyr Gln Gln Tyr Tyr Leu Arg Thr 1100 1110Ser Arg Glu Leu Arg Arg Leu Asp Ser Ile Thr Arg Ser Pro Ile 1115 1120 1125 Tyr Ser His Phe Gln Glu Thr Leu Gly Gly Leu Ala Thr Val Arg 1130 1140 Gly Tyr Ser Gln Gln Lys Arg Phe Ser His Ile Asn Gln Cys Arg 1145 1155 ile Asp Asn Asn Met Ser Ala Phe Tyr Pro Ser ile Asn Ala Asn 1160 1170 Arg Trp Leu Ala Tyr Arg Leu Glu Leu Ile Gly Ser Ile Ile Ile 1175 1180 1185

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Lys Ile Leu Val Leu Asp Glu Ala Thr Ala Ala Val Asp Val Glu 1430 1440 Thr Asp Lys Val Val Gln Glu Thr Ile Arg Thr Ala Phe Lys Asp 1455 1455 Arg Thr Ile Leu Thr Ile Ala His Arg Leu Asn Thr Ile Met Asp 1460 1460 1470 Ser Asp Arg Ile Ile Val Leu Asp Asn Gly Lys Val Ala Glu Phe 1485 Asp Ser Pro Gly Gln Leu Leu Ser Asp Asn Lys Ser Leu Phe Tyr 1490 Ser Leu Cys Met Glu Ala Gly Leu Val Asn Glu Asn Gly Gly Gly 1515 1515 Gly Gly Met Leu Ser Arg Lys Gly Ile Ile Pro Glu Glu Tyr 1520 1530 Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr Arg 1535 1540 1545 Thr Arg Glu Arg Arg Ala Arg Phe Val Ser Lys Lys Gly Asn Cys 1550 1560 Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu Gln 1565 1570 ASP Val Phe Thr Thr Leu Val ASP Leu Lys Trp Pro His Thr Leu 1580 1580 Leu Ile Phe Thr Met Ser Phe Leu Cys Ser Trp Leu Leu Phe Ala 1595 1600 1605 Met val Trp Trp Leu Ile Ala Phe Ala His Gly Asp Leu Tyr Ala 1610 1620 Tyr Met Glu Lys Gly Ile Thr Asp Leu Ala Pro Tyr Pro Tyr Asp 1625 1630 1635 Val Pro Asp Tyr Ala Gly Glu Gly Thr Asn Val Pro Cys Val Thr 1640 1645 1650

Ser Ile His Ser Phe Ser Ser Ala Phe Leu Phe Ser Ile Glu Val Page 79

Gln val Thr Ile Gly Phe Gly Gly Arg Met Val Thr Glu Glu Cys 1670 1680 Pro Leu Ala Ile Leu Ile Leu Ile Val Gln Asn Ile Val Gly Leu 1685 1690 1695 Met Ile Asn Ala Ile Met Leu Gly Cys Ile Phe Met Lys Thr Ala 1700 1710 Gln Ala His Arg Arg Ala Glu Thr Leu Ile Phe Ser Lys His Ala 1715 1720 1725 Val Ile Thr Leu Arg His Gly Arg Leu Cys Phe Met Leu Arg Val 1730 1740 Gly Asp Leu Arg Lys Ser Met Ile Ile Ser Ala Thr Ile His Met 1745 1755 Gln Val Val Arg Lys Thr Thr Ser Pro Glu Gly Glu Val Val Pro 1760 1770 Leu His Gln Val Asp Ile Pro Met Glu Asn Gly Val Gly Gly Asn 1775 1780 1785 Gly Ile Phe Leu Val Ala Pro Leu Ile Ile Tyr His Val Ile Asp 1790 1800 Ser Asn Ser Pro Leu Tyr Asp Leu Ala Pro Ser Asp Leu His His 1805 1815 His Gln Asp Leu Glu Ile Ile Val Ile Leu Glu Gly Val Val Glu 1820 1830 Thr Thr Gly Ile Thr Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp 1845 1846 Glu Ile Leu Trp Gly Gln Arg Phe Val Pro Ile Val Ala Glu Glu 1850 1860 Asp Gly arg Tyr Ser Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile 1875

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Leu Tyr Met val val Gly Thr Leu Ala Ala Ile Ile His Gly Ala Gly 50 60

Leu Pro Leu Met Met Leu Val Phe Gly Glu Met Thr Asp Ile Phe Ala 65 70 75 80

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Asp Ile Asn Asp Thr Gly Phe Phe Met Asn Leu Glu Glu Asp Met Thr 100 110

Arg Tyr Ala Tyr Tyr Tyr Ser Gly Ile Gly Ala Gly Val Leu Val Ala 115 120 125

Ala Tyr Ile Gln Val Ser Phe Trp Cys Leu Ala Ala Gly Arg Gln Ile 130 140

His Lys Ile Arg Lys Gln Phe Phe His Ala Ile Met Arg Gln Glu Ile 145 150 155 160

Gly Trp Phe Asp Val His Asp Val Gly Glu Leu Asn Thr Arg Leu Thr  $165 \ \ 175 \ \ 175$ 

Asp Asp Val Ser Lys Ile Asn Glu Gly Ile Gly Asp Lys Ile Gly Met 180 185

Phe Phe Gln Ser Met Ala Thr Phe Phe Thr Gly Phe Ile Val Gly Phe 195 200 205

Thr Arg Gly Trp Lys Leu Thr Leu Val Ile Leu Ala Ile Ser Pro Val Page 81

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215

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Phe Ser Ala Val Val Phe Gly Ala Met Ala Val Gly Gln Val Ser Ser 980 985 990 Phe Ala Pro Asp Tyr Ala Lys Ala Lys Ile Ser Ala Ala His Ile Ile Met Ile Ile Glu Lys Thr Pro Leu Ile Asp Ser Tyr Ser Thr Glu 1010 1015 1020 Gly Leu Met Pro Asn Thr Leu Glu Gly Asn Val Thr Phe Gly Glu 1025 1030 1035 Val Val Phe Asn Tyr Pro Thr Arg Pro Asp Ile Pro Val Leu Gln Gly Leu Ser Leu Glu Val Lys Lys Gly Gln Thr Leu Ala Leu Val Gly Ser Ser Gly Cys Gly Lys Ser Thr Val Val Gln Leu Leu Glu Arg Phe Tyr Asp Pro Leu Ala Gly Lys Val Leu Leu Asp Gly Lys Glu Ile Lys Arg Leu Asn Val Gln Trp Leu Arg Ala His Leu Gly 1100 1105 1110 Ile Val Ser Gln Glu Pro Ile Leu Phe Asp Cys Ser Ile Ala Glu 1115 1120 1125 ASN Ile Ala Tyr Gly ASP ASN Ser Arg Val Val Ser Gln Glu Glu 1130 1135 1140 Ile Val Arg Ala Ala Lys Glu Ala Asn Ile His Ala Phe Ile Glu Ser Leu Pro Asn Lys Tyr Ser Thr Lys Val Gly Asp Lys Gly Thr 1160 1165 1170 Gln Leu Ser Gly Gly Gln Lys Gln Arg Ile Ala Ile Ala Arg Ala Leu Val Arg Gln Pro His Ile Leu Leu Leu Asp Glu Ala Thr Ser 1190 1200 Ala Leu Asp Thr Glu Ser Glu Lys Val Val Gln Glu Ala Leu Asp

Lys Ala Arg Glu Gly Arg Thr Cys Ile Val Ile Ala His Arg Leu 1220 1225 1230 Ser Thr Ile Gln Asn Ala Asp Leu Ile Val Val Phe Gln Asn Gly 1235 1240 1245 Arg Val Lys Glu His Gly Thr His Gln Gln Leu Leu Ala Gln Lys Gly Ile Tyr Phe Ser Met Val Ser Val Gln Ala Gly Thr Lys Arg Gln Gly Gly Gly Gly Gly Met Leu Ser Arg Lys Gly Ile Ile 1280 1285 1290 Pro Glu Glu Tyr Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr Arg Thr Arg Glu Arg Arg Ala Arg Phe Val Ser Lys 1310 1315 1320 Lys Gly Asn Cys Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu Gln Asp Val Phe Thr Thr Leu Val Asp Leu Lys Trp 1340 1345 1350 Pro His Thr Leu Leu Ile Phe Thr Met Ser Phe Leu Cys Ser Trp Leu Leu Phe Ala Met Val Trp Trp Leu Ile Ala Phe Ala His Gly 1370 1380 Asp Leu Tyr Ala Tyr Met Glu Lys Gly Ile Thr Asp Leu Ala Pro 1385 1390 1395 Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Gly Glu Gly Thr Asn Val Pro Cys Val Thr Ser Ile His Ser Phe Ser Ser Ala Phe Leu Phe 1415 1420 1425 Ser Ile Glu Val Gln Val Thr Ile Gly Phe Gly Gly Arg Met Val

1210

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1535 1540 1545 Val Gly Gly Asn Gly Ile Phe Leu Val Ala Pro Leu Ile Ile Tyr 1550 1560 His Val Ile Asp Ser Asn Ser Pro Leu Tyr Asp Leu Ala Pro Ser Asp Leu His His Gln Asp Leu Glu Ile Ile Val Ile Leu Glu Gly val Val Glu Thr Thr Gly Ile Thr Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp Glu Ile Leu Trp Gly Gln Arg Phe Val Pro Ile 1610 1615 1620 Val Ala Glu Glu Asp Gly Arg Tyr Ser Val Asp Tyr Ser Lys Phe 1625 1630

Gly Asn Thr Ile Lys Val Pro Thr Pro Leu Cys Thr Ala Arg Gln  $_{1640}^{\rm ASD}$  Glu Asp Arg Ser Leu Leu Asp Ala Leu Thr Leu Ala Ser  $_{1650}^{\rm ASD}$  Gly Pro Leu Arg Lys Arg Ser Val Ala Val Ala Lys Ala  $_{1670}^{\rm ASD}$ 

Lys Pro Glu Phe Ser Ile Ser Pro Asp Ser Leu Ser 1685 1690 1695

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Pro His Val Phe Leu Leu Phe Ile Thr Phe Pro Ile Leu Phe Ile Gly

Trp Gly Ser Gln Ser Ser Lys Val Gln Ile His His Asn Thr Trp Leu

His Phe Pro Gly His Asn Leu Arg Trp Ile Leu Thr Phe Ala Leu Leu 65 70 75 80

Phe Val His Val Cys Glu Ile Ala Glu Gly Ile Val Ser Asp Ser Gln 85 90 95

Arg Ala Ser Arg His Leu His Leu Phe Met Pro Ala Val Met Gly Phe

Val Ala Thr Thr Ser Ile Val Tyr Tyr His Asn Ile Glu Thr Ser 115 120 125

Asn Phe Pro Lys Leu Leu Leu Ala Leu Phe Leu Tyr Trp Val Met Ala 130 135 140

Phe Ile Thr Lys Thr Ile Lys Leu Val Lys Tyr Trp Gln Leu Gly Trp 145 150 155 160

Gly Met Ser Asp Leu Arg Phe Cys Ile Thr Gly Val Met Val Ile Leu 165 170 175

Asn Gly Leu Leu Met Ala Val Glu Ile Asn Val Ile Arg Val Arg Arg  $180 \\ 185 \\ 190 \\$ 

Tyr Val Phe Phe Met Asn Pro Gln Lys Val Lys Pro Pro Glu Asp Leu 195 200 205

Gln Asp Leu Gly Val Arg Phe Leu Gln Pro Phe Val Asn Leu Leu Ser 210 220 Lys Ala Thr Tyr Trp Trp Met Asn Thr Leu Ile Ile Ser Ala His Arg 225 230 235 Lys Pro Ile Asp Leu Lys Ala Ile Gly Lys Leu Pro Ile Ala Met Arg 255 255 Ala Val Thr Asn Tyr Val Cys Leu Lys Glu Ala Tyr Glu Glu Gln Lys 260 270 Lys Lys Ala Ala Asp His Pro Asn Arg Thr Pro Ser Ile Trp Leu Ala 275 280 285 Met Tyr Arg Ala Phe Gly Arg Pro Ile Leu Leu Ser Ser Thr Phe Arg 290 300 Tyr Leu Ala Asp Leu Leu Gly Phe Ala Gly Pro Leu Cys Ile Ser Gly 305 310 315 ɪle val Gln Arg val Asn Glu Pro Lys Asn Asn Thr Thr Arg Phe Ser 325 335 Glu Thr Leu Ser Ser Lys Glu Phe Leu Glu Asn Ala His Val Leu Ala 340 350 Val Leu Leu Phe Leu Ala Leu Ile Leu Gln Arg Thr Phe Leu Gln Ala 355 365 Ser Tyr Tyr Val Thr Ile Glu Thr Gly Ile Asn Leu Arg Gly Ala Leu 370 380 Leu Ala Met Ile Tyr Asn Lys Ile Leu Arg Leu Ser Thr Ser Asn Leu 385 390 400 Ser Met Gly Glu Met Thr Leu Gly Gln Ile Asn Asn Leu Val Ala Ile 405 415 Glu Thr Asn Gln Leu Met Trp Phe Leu Phe Leu Cys Pro Asn Leu Trp 420 430 Ala Met Pro Val Gln Ile Ile Met Gly Val Ile Leu Leu Tyr Asn Leu 435 440 Leu Gly Ser Ser Ala Leu Val Gly Ala Ala Val Ile Val Leu Leu Ala 450 \_\_\_\_460

Pro Ile Gln Tyr Phe Ile Ala Thr Lys Leu Ala Glu Ala Gln Lys Ser 470 475 480 Thr Leu Asp Tyr Ser Thr Glu Arg Leu Lys Lys Thr Asn Glu Ile Leu 485 495 Lys Gly Ile Lys Leu Lys Leu Tyr Ala Trp Glu His Ile Phe Cys 500 510 Lys Ser Val Glu Glu Thr Arg Met Lys Glu Leu Ser Ser Leu Lys Thr 520 525 Phe Ala Leu Tyr Thr Ser Leu Ser Ile Phe Met Asn Ala Ala Ile Pro 530 540 Ile Ala Ala Val Leu Ala Thr Phe Val Thr His Ala Tyr Ala Ser Gly 545 555 560 Asn Asn Leu Lys Pro Ala Glu Ala Phe Ala Ser Leu Ser Leu Phe His 575 Ile Leu Val Thr Pro Leu Phe Leu Leu Ser Thr Val Val Arg Phe Ala 580 590 Val Lys Ala Ile Ile Ser Val Gln Lys Leu Asn Glu Phe Leu Leu Ser 505 605 Asp Glu Ile Gly Glu Asp Ser Trp Arg Thr Gly Glu Gly Thr Leu Pro 610Phe Glu Ser Cys Lys Lys His Thr Gly Val Gln Ser Lys Pro Ile Asn 625 635 640 Arg Lys Gln Pro Gly Arg Tyr His Leu Asp Asn Tyr Glu Gln Ala Arg 655 655 Arg Leu Arg Pro Ala Glu Thr Glu Asp Val Ala Ile Lys Val Thr Asn 660 665 Gly Tyr Phe Ser Trp Gly Ser Gly Leu Ala Thr Leu Ser Asn Ile Asp 675 685 lle Arg Ile Pro Thr Gly Gln Leu Thr Met Ile Val Gly Gln Val Gly 690 700 Cys Gly Lys Ser Ser Leu Leu Leu Ala Ile Leu Gly Glu Met Gln Thr Page 90

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Leu Glu Gly Lys Val Tyr Trp Asn Asn Val Asn Glu Ser Glu Pro Ser 735 730 736 Phe Glu Ala Thr Arg Ser Arg Ser Arg Tyr Ser Val Ala Tyr Ala Ala 740 745 750 Gln Lys Pro Trp Leu Leu Asn Ala Thr Val Glu Glu Asn Ile Thr Phe 755 760 765 Gly Ser Ser Phe Asn Arg Gln Arg Tyr Lys Ala Val Thr Asp Ala Cys 770 775 780 Ser Leu Gln Pro Asp Ile Asp Leu Leu Pro Phe Gly Asp Gln Thr Glu 785 795 800 Ile Gly Glu Arg Gly Ile Asn Leu Ser Gly Gly Gln Arg Gln Arg Ile 805 815 Cys val Ala Arg Ala Leu Tyr Gln Asn Thr Asn Ile Val Phe Leu Asp 820 825 830 ASP Pro Phe Ser Ala Leu ASP Ile His Leu Ser ASP His Leu Met Gln 835 840 845 Glu Gly Ile Leu Lys Phe Leu Gln Asp Asp Lys Arg Thr Val Val Leu 850 860 Val Thr His Lys Leu Gln Tyr Leu Thr His Ala Asp Trp Ile Ile Ala 865 870 880 Met Lys Asp Gly Ser Val Leu Arg Glu Gly Thr Leu Lys Asp Ile Gln 885 890 Thr Lys Asp Val Glu Leu Tyr Glu His Trp Lys Thr Leu Met Asn Arg  $900 \hspace{1.5cm} 900 \hspace{1.5cm} 901 \hspace{1.5cm}$ Gln Asp Gln Glu Leu Glu Lys Asp Met Glu Ala Asp Gln Thr Thr Leu 925 925 Glu Arg Lys Thr Leu Arg Arg Ala Met Tyr Ser Arg Glu Ala Lys Ala 930 940 Gln Met Glu Asp Glu Asp Glu Glu Glu Glu Glu Glu Asp Glu Asp 945 950 960

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Asn Phe Ser val Gly Gln Arg Gln Leu Phe Cys Leu Ala Arg Ala 1445 $$1455$$	
Phe Val. arg Lys Ser Ser Ile Leu Ile Met Asp Glu. Ala Thr Ala $1460$	
Ser Ile Asp Met Ala Thr Glu Asn Ile Leu Gln Lys Val Val Met 1475 $$1485\ $	
Thr Ala Phe Ala Asp arg Thr Val Val Thr Ile Ala His Arg Val 1490 $$1500\ $	
Ser Ser Ile Met Asp Ala Gly Leu Val Leu Val Phe Ser Glu Gly 1505 1515	
Ile Leu Val Glu Cys Asp Thr Gly Pro Asn Leu Leu Gln His Lys 1520 1530	
Asn Gly Leu Phe Ser Thr Leu $$ Val Met Thr Asn Lys Gly Gly Gly 1535 $$ 1540 $$	
Gly Gly Met Leu Ser Arg. Lys Gly Ile Ile Pro. Glu Glu Tyr. $1550 \\$	
Val Leu Thr Arg Leu Ala Glu Asp Pro Ala Glu Pro Arg Tyr Arg 1575	
Thr arg Glu arg arg ala arg Phe val Ser Lys Lys Gly Asn Cys 1580 1590	
Asn Val Ala His Lys Asn Ile Arg Glu Gln Gly Arg Phe Leu Gln $1595 \\ 1600 \\ 1605$	
Asp Val Phe Thr Thr Leu Val Asp Leu Lys Trp Pro His Thr Leu $1610 \\ 1610$	
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Met Val Trp Trp Leu Ile Ala Phe Ala His Gly ASP Leu Ala Pro $1640$ $1650$	
Gly Glu Gly Thr Asn Val Pro Cys Val Thr Ser Ile His Ser Phe $1655 \\ 1660$	
Ser Ser Ala Phe Leu Phe Ser Ile Glu Val Gln Val Thr Ile Gly Page 94	

Phe Gly Gly Arg Met Val Thr Glu Glu Cys Pro Leu Ala Ile Leu 1685 1690 1695 Ile Leu Ile Val Gln Asn Ile Val Gly Leu Met Ile Asn Ala Ile 1700 1705 1710 Met Leu Gly Cys Ile Phe Met Lys Thr Ala Gln Ala His Arg Arg Ala Glu Thr Leu Ile Phe Ser Lys His Ala Val Ile Thr Leu Arg His Gly Arg Leu Cys Phe Met Leu Arg Val Gly Asp Leu Arg Lys 1745 1750 1755 Ser Met Ile Ile Ser Ala Thr Ile His Met Gln Val Val Arg Lys 1760 1765 1770 Thr Thr Ser Pro Glu Gly Glu Val Val Pro Leu His Gln Val Asp 1775 1780 1785 Ile Pro Met Glu Asn Gly Val Gly Gly Asn Gly Ile Phe Leu Val Ala Pro Leu Ile Ile Tyr His Val Ile Asp Ser Asn Ser Pro Leu 1805 1810 1815 Tyr Asp Leu Ala Pro Ser Asp Leu His His His Gln Asp Leu Glu Ile Ile Val Ile Leu Glu Gly Val Val Glu Thr Thr Gly Ile Thr 1835 1840 1845 Thr Gln Ala Arg Thr Ser Tyr Leu Ala Asp Glu Ile Leu Trp Gly 1850 1855 1860 Gln Arg Phe Val Pro Ile Val Ala Glu Glu Asp Gly Arg Tyr Ser 1865 1870 1875 Val Asp Tyr Ser Lys Phe Gly Asn Thr Ile Lys Val Pro Thr Pro 1880 1885 1890 Leu Cys Thr Ala Arg Gln Leu Asp Glu Asp Arg Ser Leu Leu Asp 1895 1900 1905

1675

Ala Le 19	u Thr 110	Leu	Ala	Ser	Ser 1915	Arg		63US: Pro			Lys	Arg	Ser		
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<212> PRT
<213> artificial sequence
<220>
<223> HA epitope
<400> 23
Tyr Pro Tyr Asp Val Pro Asp Tyr Ala
<210> 24
<211> 11
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<400> 24
Asp Leu Tyr Ala Tyr Met Glu Lys Gly Ile Thr 1 	 5 	 10
<210> 25
<211> 6
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<223> export signal
<400> 25
Phe Cys Tyr Glu Asn Glu
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